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IN THE

Supreme Court of the United States

OCTOBER TERM, 1972

No. 72-666

USV PHARMACEUTICAL CORPORATION, PETITIONER

v.

CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION AND WELFARE, AND CHARLES C. EDWARDS, COMMISSIONER OF FOOD AND DRUGS

On Writ of Certiorari to the United States Court of Appeals for the Fourth Circuit

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BRIEF FOR PETITIONER

OPINIONS BELOW

The opinion of the court of appeals (A. 466-73) is reported at 461 F.2d 223. The opinion of the district court (A. 463-66) is not officially reported, but is reprinted at CCH FOOD DRUG COSM. L. REP. ¶ 40,489.

JURISDICTION

The judgment of the court of appeals (A. 474) was entered on May 24, 1972. A petition for rehearing was denied on July 5, 1972. The Chief Justice extended until October 30, 1972, the time within which to file a petition for certiorari. The petition was filed on October 30, 1972, and was granted on January 8, 1973 (409 U.S. —). The jurisdiction of this Court rests upon 28 U.S.C. § 1254(1). *Abbott Labs.* v. *Gardner,* 387 U.S. 136 (1967).

STATUTES INVOLVED

Section 201(p) of the Federal Food, Drug and Cosmetic Act of 1938, 52 Stat. 1041, provided in pertinent part:

> (p) The term "new drug" means—
>
> (1) Any drug the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a "new drug" if at any time prior to the enactment of this Act it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or
>
> (2) Any drug the composition of which is such that such drug, as a result of investigations to determine its safety for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

The Drug Amendments of 1962, 76 Stat. 781, 788-89, 21 U.S.C. § 321(p), note foll. § 321, provide in pertinent part:

> Sec. 102. (a)(1) Section 201(p)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321 (p)(1)), defining the term "new drug", is amended by (A) inserting therein, immediately after the words "to evaluate the safety", the words "and effectiveness",

and (B) inserting therein immediately after the words "as safe", the words "and effective".

(2) Section 201(p)(2) of such Act (21 U.S.C. 321(p)(2)) is amended by inserting therein, immediately after the word "safety", the words "and effectiveness".

Sec. 107. * * *

(c) * * *

(4) In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

The pertinent provisions of Section 505 of the Federal Food, Drug, and Cosmetic Act of 1938, 52 Stat. 1052, as originally enacted and in force until October 10, 1962, are set forth at pp 1a-3a *infra*.

QUESTIONS PRESENTED

The 1962 amendments to the Federal Food, Drug, and Cosmetic Act of 1938 expanded the statutory definition of "new drugs", for which a new drug application ("NDA") must be approved by the Food and Drug Administration in advance of marketing, to include drugs "not generally recognized as * * * effective * * *" in addition to those "not generally recognized * * * as safe * * *". A "grandfather" provision, however, exempted drugs already on the market which then were not "new drugs", as defined by the Act prior to amendment, and "not covered by an effective [new drug] application * * *".

The questions are:

1. Whether the "grandfather" provision applies to pre-1962 drugs which were never "new drugs" from the mo-

ment of their introduction and were never the subject of a new drug application, thus literally qualifying for "grandfathered" status under the precise terms of the provision, but which are "me-too" products comprised of the same principal ingredient as earlier products of the same manufacturer for which NDA's had originally been filed.[1]

2. Whether the "grandfather" provision applies to pre-1962 drugs which had been the subject of an NDA when first introduced, but which by the time of the 1962 amendments were concededly no longer "new drugs", and were being treated by both the manufacturer and FDA as no longer subject to the regulatory scheme applicable to NDA'd products.

STATEMENT

The history of the products involved. In late 1955 and early 1956 petitioner USV Pharmaceutical Corp. filed new drug applications ("NDA's") with the Commissioner of Food and Drugs for a line of five drug products containing citrus flavonoid compound, a natural chemical substance extracted from citrus fruit (A. 368, 371).[2] The

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[1] In this Court the government has confessed error with respect to the rationale of the ruling below in its favor on this question, "agree[ing] with petitioner that the distinction drawn [by the court of appeals] between USV's me-toos and those of its competitors is discriminatory and not supportable" (Resp. Mem. on Petition for Certiorari (hereafter "Resp. Mem."), p. 11 n.13). But, by urging affirmance on a ground repudiated by the court of appeals, the government raises a broader question, *i.e.*, whether the "grandfather" provision applies to any "me-too" products, whether or not made by the same manufacturer as the pioneer formerly NDA'd product (see *id.*, p. 6). Petitioner will address the government's proposed issue in the Argument portion of this brief, as well as the narrower question presented by the petition for certiorari.

[2] The products were CVP Capsules; CVP Syrup; CVP with Vitamin K Syrup; CVP with Vitamin K Tablets; and Duo-CVP Capsules.

recommended use of the products was, and continues to be, control of abnormal capillary permeability and fragility (A. 394, 396, 425).[3]

Under the pre-1962 statutory scheme then in force, an effective NDA was the legal prerequisite for marketing a "new drug",[4] that is, a drug which (1) was "not generally recognized by experts * * * as safe" for its intended uses or (2) if generally so recognized but only as a result of investigations, had not otherwise been used to a material extent or for a material time.[5] A filed NDA automatically became effective after sixty days (or one hundred-eighty days if so ordered by the Commissioner), unless within that time the Commissioner issued an order refusing to permit the NDA to become effective.[6] In the NDA the manufacturer was required to show that his product was in fact safe, and the Commissioner's decision not to take action constituted tacit ratification of such proof.

In the present case the Commissioner took no action to block the effectiveness of USV's citrus flavonoid new drug applications. They consequently became effective sixty

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[3] This is a condition of the capillary walls which may result in easy surface bleeding such as bruises (A. 384, 435, 442-43). The use of USV's citrus flavonoid products for this purpose is recommended to physicians only. While no prescription is required to purchase these products, they are described merely as "a supplementary source of bioflavonoids" in the labeling made available to the lay purchaser. (A. 389-90.)

[4] Federal Food, Drug, and Cosmetic Act of 1938, § 505(a), 52 Stat. 1052. As amended in 1962 (Drug Amendments of 1962, § 104(a), 76 Stat. 784, 21 U.S.C. § 355(a)), § 505(a) now requires that an "approval" of a new drug application be effective.

[5] Section 201(p), 52 Stat. 1041.

[6] Section 505(c), 52 Stat. 1052. As amended in 1962 (Drug Amendments of 1962, § 104(c), 76 Stat. 784, 21 U.S.C. § 355(c)), § 505(c) now requires the Commissioner affirmatively to approve the new drug application before a new drug may be marketed.

days after filing, and the products were accordingly placed on the market (A. 366, 368).

In 1957 USV developed two additional citrus flavonoid products, similar in composition and labeling to the five for which NDA's had become effective the preceding year (A. 368, 465).[7] After obtaining explicit advice from the Food and Drug Administration as to one of the proposed products [8] that it was "generally recognized as safe", and hence was not a "new drug" within the meaning of the statute, USV began to market these "me-too" drugs without filing NDA's therefor (A. 368).[9] This action was never challenged by the agency (A. 369).

In 1961 USV sought a comparable Food and Drug Administration ruling as to its originally NDA'd citrus flavonoid products (A. 299). In response, FDA advised that two of the NDA'd products "are not new drugs". As to the remainder, FDA replied that it had incomplete current marketing information on which to base a determination, but would be "pleased" to rule upon receipt of additional data. (A. 300-01.)

USV supplied the requested information within a month, noting its "recollection" that "a short time after the NDA

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[7] The new products were Bivam, and Duo-CVP with Vitamin K Capsules. No additional labeling directed to physicians recommending Bivam for abnormal capillary permeability and fragility was disseminated.

[8] No separate ruling was sought on Duo-CVP with Vitamin K Capsules.

[9] In the regulatory parlance, as the court of appeals found, a "me-too" drug is one substantially identical to a previously-marketed product for which an NDA has become effective (since 1962, has been approved) but which subsequently became generally recognized as safe (and, since 1962, as efficacious), with the result that the copy is not a "new drug" within the meaning of the statute and can therefore be marketed without an effective (since 1962, approved) NDA. See A. 470, 472.

became effective" (*i.e.*, in 1956-57) its citrus flavonoid products were no longer considered to be "new drugs". "Confirmation of the above" was requested. (A. 301.) FDA never responded.

It has traditionally been considered the responsibility of the manufacturer to decide, subject to severe penalties if he is later held to have decided incorrectly, whether his product is a "new drug" requiring pre-marketing approval by FDA.[10] Because the identical citrus flavonoid compound was contained in all USV bioflavonoid products, three of which FDA had expressly ruled were not "new drugs", USV concluded that the "not-new" status of all these products had been established, and thereafter discontinued filing with FDA the supplemental information then required by regulations[11] as to NDA'd products (A. 301-02, 451). Although FDA was thus fully aware of USV's position that the products were no longer "new drugs" within the meaning of the statute, and that the company was treating each of them as no longer subject to the regulatory scheme applicable to NDA'd products, this too was never challenged by the agency.

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[10] *Bentex Pharmaceuticals, Inc.* v. *Richardson*, 463 F.2d 363, 365-66 (4th Cir. 1972), *cert. granted*, 409 U.S. — (1973) (No. 72-555) (A. 260). See also Peter Barton Hutt, *Proper Classification of Products under the Federal Food, Drug, and Cosmetic Act*, p. 3 (unpublished paper presented at Annual Convention of the Federal Bar Ass'n, Miami, Fla., Sept. 4, 1969). ("The third, and final, general principle is that it is the primary and initial responsibility of the manufacturer of a product to determine the proper classification of his product, and to make certain that it meets all applicable legal requirements. It is in no instance necessary, and in most instances inadvisable, to ask the Food and Drug Administration for its opinion on the proper classification of the product. • • • It is • • • usually preferable for the manufacturer to exercise the obligation of proper classification given to him by the statute, rather than abdicating that responsibility to the Government.")

[11] Section 130.9, 25 Fed. Reg. 12595 (1960).

The Drug Amendments of 1962. In 1962, the Kefauver-Harris amendments to the Food, Drug, and Cosmetic Act expanded the grounds upon which the marketing of a "new drug" could be prevented or terminated by FDA. Prior to 1962, a new drug application could be prevented from becoming effective, and its effectiveness could thereafter be suspended, only on grounds relating to safety.[12] The 1962 amendments required FDA, in deciding whether to approve or to revoke approval of new drug applications, to consider the evidence of efficacy as well.[13] At any time after the expiration of a two-year "grace period", moreover, FDA could initiate revocation proceedings as to pre-1962 NDA's which were still operative [14] and, after "due notice and an opportunity for hearing to the applicant", withdraw approval previously granted upon a finding "that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have * * *".[15]

The 1962 amendments also expanded the definition of "new drug" to cover drugs not generally recognized by experts as "safe *and effective*" for their intended uses.[16] However, as to certain products already on the market and generally recognized as safe, Section 107(c)(4) of the amending statute granted "grandfather" exemption from the definition of "new drug" as amended, and preserved the right of such products to remain on the market without advance FDA approval. To qualify for the Section 107

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[12] Sections 505(d), -(e), 52 Stat. 1052-53.

[13] Drug Amendments of 1962, §§ 102(c), -(d), 76 Stat. 781-82, 21 U.S.C. §§ 355(d), -(e).

[14] Drug Amendments of 1962, § 107(c)(3), 76 Stat. 788-89, 21 U.S.C. note foll. § 321.

[15] Drug Amendments of 1962, § 102(d), 76 Stat. 782, 21 U.S.C. § 355(e).

[16] Drug Amendments of 1962, §§ 102(a)(1), -(2), 76 Stat. 781, 21 U.S.C. § 321(p) (emphasis added).

(c)(4) exemption, it must be shown that the product "on the day immediately preceding the enactment date" (*i.e.*, October 9, 1962) satisfied three conditions: (A) that it was commercially used or sold in the United States, (B) that it was not a "new drug" as defined by the Act as then in force (*i.e.*, was "generally recognized * * * as safe" and had been used for a material time and extent), and (C) that it was not "covered by an effective [new drug] application" under the Act.[17]

Continued exemption of a "grandfathered" product from the FDA preclearance requirement does not mean that the public is unprotected against an ineffective drug. False or misleading efficacy claims constitute "misbranding" in violation of the Act, as they have since 1938, and subject the manufacturer to severe criminal and civil sanctions as well as seizure of his product and its removal from the market.[18]

The origins of the present litigation. In July 1968, relying upon an adverse report on the efficacy of one of USV's bioflavonoid products rendered by the National Academy of Sciences/National Research Council Drug Efficacy Study which FDA had commissioned following the 1962 amendments,[19] FDA initiated proceedings under the Act as amended[20] to revoke approval of the three citrus flavonoid NDA's held by USV. In light of FDA's

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[17] 76 Stat. 789, 21 U.S.C. note foll. § 321.

[18] § 502(a), 52 Stat. 1050, 21 U.S.C. § 352(a). *See Bentex Pharmaceuticals, Inc.* v. *Richardson*, note 10 *supra*, 463 F.2d at 367 (A. 262). See also note 151 *infra*.

[19] A. 290. The particular Drug Efficacy Study report relied on by FDA has since been condemned as "cryptic and conclusory, without any statement of supporting facts" (*USV Pharmaceutical Corp.* v. *Secretary of HEW*, 466 F.2d 455, 461 (D.C. Cir. 1972)).

[20] Section 505(e), 52 Stat. 1053, *as amended*, 21 U.S.C. § 355(e).

prior position with regard to the products, however, the company believed that each of its citrus flavonoid formulations satisfied the criteria for "grandfathered" status under Section 107(c)(4) of the 1962 amendments and that, under the pre-1962 definition of "new drug" which therefore remained applicable, the products were not "new drugs" for which an approved NDA was in any event required.

Petitioner therefore instituted the present action in the district court for a declaratory judgment to that effect against the Secretary of Health, Education and Welfare and the Commissioner of Food and Drugs, who are charged with the administration of the Food, Drug, and Cosmetic Act.[21] A stay of the administrative revocation proceeding for the pendency of the declaratory judgment action was sought from FDA.[22]

The decision of the district court. After a full evidentiary trial, the district court issued its findings and con-

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[21] Section 201(d), 52 Stat. 1040, *as amended*, 21 U.S.C. § 321(d); 21 C.F.R. § 2.120.

[22] The stay was denied, but no further action was taken by FDA to prosecute the revocation proceeding. In July 1970, contemporaneously with the setting of a trial date in the declaratory judgment action, FDA sought to revive the revocation proceeding by calling upon petitioner to establish its right to a hearing under "summary judgment" regulations which the agency had promulgated in the interim. Petitioner again moved for a stay pending disposition of the declaratory judgment action (A. 302-04). Eight days before trial in the district court was scheduled to begin, FDA denied the stay and entered a final order of revocation, refusing to allow petitioner to contest the matter further (A. 297-99, 304-05). The revocation order has since been set aside by the Court of Appeals for the District of Columbia Circuit for denial of "administrative due process", resulting from FDA's use of procedures which were "fundamentally defective • • • unsound and unfair" (*USV Pharmaceutical Corp.* v. *Secretary of HEW*, note 19 *supra*, 466 F.2d at 460, 461). No review in this Court was sought (see Resp. Mem., p. 4 n. 6).

clusions in the form of an Order and Memorandum Opinion (A. 463-66). FDA's challenge to jurisdiction was rejected on the authority of this Court's decision in *Gardner* v. *Toilet Goods Ass'n*, 387 U.S. 167 (1966) (A. 464). Proceeding to the merits, the court held that petitioner was correct as to all its citrus flavonoid products—both the "me-too" products for which no NDA had ever been filed, and also those products for which NDA's had become effective when the products were originally introduced.

The court found Clauses (A) and (B) of Section 107(c)(4) to be satisfied as to each of the products—they were on the market prior to the 1962 amendments (A. 464), and at that time they were not "new drugs" (A. 465). And as to the "me-too" products, the district court ruled that they "were never covered by effective new drug applications", thus qualifying under Clause (C) as well (A. 464).

As to the formerly NDA'd products, the court found that by the time of the 1962 amendments both petitioner and FDA were treating the products as no longer subject to the regulatory scheme applicable to NDA'd products. Thus, in a practical sense, the previously-approved NDA's had been effectively withdrawn by petitioner, and "none of the plaintiff's bioflavonoid products in question were covered by an effective NDA as of October 9, 1962." (A. 464-465.)

Clause (C) of Section 107(c)(4) was therefore satisfied in the case of the formerly NDA'd products as well, and the pre-amendment definition of "new drug" continued to apply (A. 463), under which the products were not "new drugs" (A. 462). The remedy for any misleading claims of efficacy, the district court concluded, thus continued to be in criminal, injunction and seizure actions for unlawful "misbranding", rather than in administrative denial or revocation of marketing authority by FDA (A. 463).

The decision of the court of appeals. On appeal, after summarily affirming the jurisdictional ruling below (A.

467),[23] the court of appeals considered separately the NDA'd and non-NDA'd drugs. Although both groups were found to satisfy Clauses (A) and (B) of Section 107 (c)(4), the court reversed the ruling of the district court under Clause (C) as to both the "me-too" and the formerly NDA'd products.

(a) Dealing first with the formerly NDA'd products, the court of appeals rejected the district court's findings that the NDA's "had been effectively and practically withdrawn and that accordingly the drugs were not covered by an effective NDA" on October 9, 1962 (A. 468). "The error in this reasoning", the court stated, "is that it assumes that a manufacturer may effect a withdrawal of an effective NDA, either by a formal notice or by discontinuing compliance with the reporting requirements for NDA'd drugs. * * * [H]e has no such right after approval of the application by the Secretary. At that point, only the Secretary can withdraw the approval." Since the Secretary had undertaken no action to withdraw approval of petitioner's applications, the formerly NDA'd products were still covered. (A. 469.)

The court of appeals additionally rejected an alternative theory which it thought to be implicit in petitioner's argument: that since all the products involved had concededly become "generally recognized * * * as safe" prior to October 9, 1962, they had ceased to be "new drugs" and therefore the previously issued NDA's were no longer needed or 'effective' ". This theory, the court said, "would make surplusage of requirement (C) in the exemption statute" and by thus treating (C) as a "nullity" would offend "the well settled rule of statutory construction that all parts of a statute are to be given effect if at all possible." (A. 469-70.)

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[23] The court of appeals invoked by reference the rationale it had set out in the companion case of *Bentex Pharmaceuticals, Inc.* v. *Richardson*, note 10 *supra*.

(b) The court acknowledged that a separate problem existed as to USV's two non-NDA'd "me-too" products. Under the plain language of Section 107(c)(4), the products were "grandfathered" since they were admittedly "generally recognized * * * as safe" from the outset and had *never* been "covered" by an effective NDA (A. 470). Moreover, most commentators, while admitting the "incongruity" of a result which would exempt "me-too" products from the amended definition of "new drug" but not their pioneer NDA'd products, considered the result "compelled by the literal language of the statute." FDA's contention to the contrary in the course of this litigation had already been "severely criticized and with considerable reason." The argument was "at variance with the uniform position [FDA] has taken over the years with regard to the nature of NDA's", which, simply stated, was the NDA is "personal" to drugs "as individual articles, not as collective groups". (A. 470-71.)

Yet, having thus concluded that "me-too" versions generally are embraced by Section 107(c)(4), the court of appeals ruled that petitioner's own "me-too's" are not. The court reasoned that petitioner's "me-too's" were "similar in formula and labeling" to its earlier NDA'd drugs; that these NDA's were "personal" to petitioner; and that the NDA's therefore "covered" not only the specific NDA'd products but also "all others like in formula" subsequently manufactured by petitioner. The two non-NDA'd products were thus also found to be derivatively ineligible for "grandfathered" status despite the literal language of the statute to the contrary. (A. 473.)

(c) Because each of petitioner's pre-1962 citrus flavonoid products is in all likelihood a "new drug" under the statutory definition as amended, the effect of the court's decision that the amended definition applies is to make an approved NDA prerequisite to the continued marketing of each product, whether or not an effective NDA was ever

necessary prior to 1962. The court conceded that "this conclusion places [petitioner] in a less favorable position than [other manufacturers] who may have copied its product prior to October 9, 1962". But the inequity thus created could be redressed, the court held, only by Congress. (A. 473.)

INTRODUCTION AND SUMMARY OF ARGUMENT

While the issues in this case involve solely the interpretation of the "grandfather" provisions of the Drug Amendments of 1962, those provisions are inextricably intertwined with other strands of the complex regulatory scheme established by Congress in the Federal Food, Drug, and Cosmetic Act. As has been said with reference to other sections of this "long and complicated" statute, the "grandfather" provisions "do not stand entirely separate and independent of the Act's structure."[24] Enacted against a background of almost twenty-five years of Food and Drug Administration interpretation and enforcement of the basic 1938 statute—a background with which Congress was made closely familiar through extensive committee hearings and reports on the proposed amendments—the 1962 "grandfather" provisions cannot be construed *in vacuo*. They must be read in the context of the entire regulatory structure erected by Congress in 1938, the substantive revisions made in 1962, and the purposes which the legislative history shows were intended to be served by those revisions as well as the alternative purposes which Congress considered and rejected.

In seeking to confine the 1962 "grandfather" provisions as narrowly as possible, the government does more than merely ignore the language of the statute expressly conferring "grandfathered" status upon pre-1962 products which, like petitioner's, were not then "covered by an effec-

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[24] *United States* v. *Sullivan*, 332 U.S. 689, 699 (1948) (Rutledge, J., concurring).

tive [new drug] application". It presses upon the court a construction which would distort the basic elements of the regulatory scheme devised by Congress in 1938 and continued in 1962. The government's proposed construction of the "grandfather" provisions would introduce fundamental inconsistencies and conflicts into the regulatory structure, and would nullify Congress' carefully considered 1962 decision (1) to continue to regulate "new drugs" differently from other drugs, and (2) to preserve the "old drug" status of products already on the market which, like those of petitioner, were not then being regulated under the 1938 statute as "new drugs".

The products involved in this case were all on the market prior to 1962, when the "new drug" regulatory provisions were expanded to include FDA pre-marketing review of drug efficacy as well as safety. Some of petitioner's products had previously been regulated as "new drugs", under the former statutory provisions for FDA pre-marketing review of safety; others had from the outset been "old drugs" generally recognized as safe, and therefore had always been regulated solely through the parallel system of civil and criminal remedies provided by Congress for dealing with such products rather than through the "new drug" provisions.

The 1962 amendments enlarged the statutory definition of the term "new drug", and in the absence of any "grandfather" provisions would have converted many "old drugs" then on the market into "new drugs" requiring Food and Drug Administration approval if their marketing were to continue. The legislative history of the 1962 amendments unambiguously demonstrates, however, that this was not Congress' purpose. Products already on the market and then being regulated not as "new drugs" but as "old drugs", like petitioner's here, were to continue to be regulated under the provisions of the Act applicable to "old drugs" so long as no new claims for the products

were made. This was accomplished by including in the 1962 statute a carefully worded "grandfather" clause limiting the applicability of the amended "new drug" definition.

The district court in the present case held that the "old drug" status of each of petitioner's pre-1962 products was protected by these "grandfather" provisions. The court of appeals held that none of the products was protected, but rested its ruling as to some of them on a ground now repudiated by the government, which seeks to defend the decision below on an alternative theory which both the district court and the court of appeals in this case have considered and rejected.

I. Two of petitioner's citrus flavonoid products were never the subject of effective NDA's. These products were introduced after other but similar products, manufactured by petitioner and originally marketed under effective NDA's, had become "generally recognized as safe" and therefore no longer were "new drugs". Petitioner marketed these "me-too" products from the outset as "old drugs"; they never were regulated under the provisions applicable to "new drugs".

As the court of appeals correctly observed, most "me-too" products such as petitioner's qualify for "grandfathered" status, because under the literal terms of the statute they were never "covered" by an effective NDA. But because petitioner itself had earlier marketed other citrus flavonoid products containing the same principal ingredient, under effective NDA's, the court of appeals held that, under the long-established doctrine that an NDA is "personal" to the manufacturer submitting the application, petitioner's effective NDA's "would cover all its products similar in formula, including those specifically described in its applications and all others like in formula."

This ruling that an NDA radiates out to all similar products of the applicant, even though competing manufacturers' "me-too" versions of the same drug are not

"covered", overlooks one of two co-equal aspects of the "personal NDA" doctrine—that the NDA is personal not only to the manufacturer but to the specific product described in the application as well. In this Court, the government concedes that the distinction drawn by the court of appeals on the basis of whether the manufacturer in question held the pioneer NDA is "discriminatory and not supportable", but urges that "grandfathered" status should be denied to *any* "me-too" product similar in composition and use to another product which itself was covered by an effective NDA, no matter by whom manufactured.

This broad proposition was properly rejected by the court of appeals as in conflict with "the consistent construction of the Act by the FDA for thirty years * * * which accords with the literal language of the Act * * * [and therefore] may only be changed by Congress itself." On their face, the "new drug" provisions of the statute apply solely to "the applicant" under an NDA; the statute has never conferred any procedural rights upon other manufacturers to participate in or to seek judicial review of the adjudicatory proceedings conducted by FDA to determine whether the showing necessary to market the product has been made, or whether marketing rights enjoyed under an NDA should be revoked. The Food and Drug Administration has repeatedly asserted, in a variety of contexts, that an effective NDA confers marketing authority on no one but the applicant, and only for the products precisely as described in the application.

Moreover, by now suggesting for the first time in the thirty-five year history of the Act that authority to market a "me-too" product without filing an NDA derives from a previous NDA for some other but similar product, the government ignores the critical statutory distinction between *evidence* of the product's safety (or efficacy), which must be shown to the satisfaction of the Food and Drug Administration by the manufacturer if his product is a "new drug" for which an NDA is required, and *general*

expert recognition of safety (or efficacy)—an entirely different standard which must be met if the product is sought to be marketed without an NDA as an "old drug." The government's present assertion further ignores the long-held position of FDA that, under the "new drug" provisions of the statute, all variations in the dosage form, quantity, and combinations in which a product may be manufactured must be separately considered in deciding whether a particular variation is a "new drug" and in determining whether its marketing should be allowed.

These crucial elements of the regulatory scheme—which would be turned topsy-turvy if the government's present construction of the "grandfather" provisions were accepted—were expressly communicated to Congress by FDA during the legislative consideration of the 1962 amendments. The wholly "personal" character of an effective NDA, both as to the applicant as manufacturer and as to the precise form of the product described in the NDA, was a fundamental, unquestioned premise upon which Congress acted when it adopted the "grandfather" provisions. Moreover, Congress' understanding of this premise, and its acceptance of it for the future as well as in construing the basic 1938 statute, is manifest from other provisions in the 1962 amendments which are integrally related to the "new drug" regulatory scheme. In these circumstances, the government's conceded "reinterpretation" of the nature and effect of a pre-1962 effective NDA would work an unsupportable alteration of the fundamental structure of "new drug" regulation established by Congress.

Nor would such a "reinterpretation" be warranted by anything in the "purposes" of the 1962 amendments. Apart from the fact that nothing in those purposes could retroactively alter the meaning of the statute as enacted in 1938, the purpose which is relevant to this case is the one which led Congress to amend the definition of "new drug". That purpose, explicitly reiterated throughout the legislative

history, was not to impose "new drug" regulatory controls on existing claims for products already on the market which, like those of petitioner, were then being regulated solely as "old drugs". It was, rather, to insure that future claims for such products, and all claims for products subsequently introduced (whether made in the initial marketing or at some time thereafter), would be regulated under the scheme applicable to "new drugs" if the product were not generally recognized as both safe and effective for that claim. The government's apparent premise that expansion of the "new drug" category to include pre-existing "me-too" products would be desirable, from a regulatory standpoint, furnishes no warrant for judicial enlargement of the amended definition of "new drug" beyond what Congress intended to accomplish, and in contravention of the express terms of the "grandfather" provisions.

II. Although the court of appeals was thus clearly correct in rejecting the broad proposition advanced by the government as to "me-too" products, and erred in that regard only in excluding petitioner's "me-too's" from the scope of its ruling, the court misapprehended the nature of the "new drug" regulatory scheme in also holding that petitioner's formerly NDA'd products were outside the scope of the "grandfather" provisions.

Congress' purpose never extended to the imposition of "new drug" controls on existing claims for products already on the market which were not then being regulated as "new drugs". And the district court found on the undisputed facts that petitioner's actions after its original NDA's had become effective—actions which were affirmed or acquiesced-in by FDA—amounted in practical terms and legal effect to withdrawal of the NDA's, with consequent termination of NDA coverage, prior to the enactment of the 1962 amendments.

The court of appeals, apparently misled by its assumption that the acronym "NDA" stands for "New Drug Approval" rather than for "New Drug Application", con-

cluded that withdrawal of the *NDA*, by petitioner, was foreclosed by the power of FDA to withdraw *approval* under Section 505(e) of the statute as amended in 1962. But the statute has never empowered FDA to terminate the coverage of an NDA on the ground that the drug involved has become an "old drug" which, because it has become "generally recognized as safe" through use for a material time and extent, need no longer be subject to "new drug" regulation. The Food and Drug Administration's authority under Section 505(e) permits it to act only for the very opposite reason—that there is no longer evidence showing the product to be safe (or, under the amended statute, efficacious).

If an effective NDA which has become superfluous may be retired on that ground (and common sense says it may and should), then the procedure for doing so must be inferred from the whole scheme and purpose of the statute. And it strains both reason and common sense to hold that though the "no longer new" status of a product has been (a) asserted by the manufacturer, (b) ratified by FDA, (c) acted upon by the manufacturer (in discontinuing all supplemental NDA filings) and (d) put into practical effect by FDA (in no longer imposing NDA controls), the product is nevertheless still "covered by an effective [new drug] application" for purposes of the "grandfather" provisions because there has been no resort to the formal revocation-of-approval procedures of Section 505(e), which can be initiated only by FDA, extend only to the precisely opposite situation, and therefore could not have been invoked by petitioner to terminate the coverage of its NDA's on the ground that the products were no longer "new".

The district court was therefore correct in construing the "grandfather" provisions of the 1962 amendments to embrace petitioner's formerly NDA'd but no longer "new" products, as being among those not "covered by an effective NDA" when the amendments were enacted. As thus con-

strued, no part of the 1962 "grandfather" provisions is surplusage. To the contrary, the government's proposed construction, taken as a whole, would in practical terms read the provisions entirely out of the statute, by confining their operation to those products already on the market when the basic Act was enacted in 1938 and, accordingly, already protected by the original 1938 "grandfather" clause which was left undisturbed by Congress in 1962.

In sum, the government's effort in this case to rewrite the 1962 "grandfather" provisions, so as to win from this Court what FDA requested but was unable to obtain from Congress, is justified by none of the familiar aids to statutory construction. It would result only in a regulatory hodgepodge bearing no resemblance to the carefully balanced scheme which Congress established in 1938 and continued in 1962 without basic structural departures.

ARGUMENT

I. THE COURT OF APPEALS CORRECTLY CONSTRUED THE "GRANDFATHER" PROVISIONS OF THE 1962 AMENDMENTS IN ACCORDANCE WITH THEIR TERMS, SO AS TO PRESERVE THE ORIGINAL DEFINITION OF "NEW DRUG" FOR PRE-1962 "ME-TOO" PRODUCTS FOR WHICH NO NDA'S HAD EVER BEEN FILED BY THEIR MANUFACTURERS, AND ERRED ONLY IN DISCRIMINATORILY DENYING THE BENEFIT OF THIS RULE TO PETITIONER.

A. The Government Has Abandoned Its Dispute with Petitioner as to the Facts and Has Confessed Error as to the Rationale of the Decision Below on the Legal Issue.

As described above (p. 6 *supra*), Bivam and Duo-CVP with Vitamin K Capsules contain the same citrus flavonoid compound as certain earlier products of petitioner for which NDA's had originally been filed and become effective. They were first marketed by petitioner in 1957 after securing an informal opinion from the Food and Drug Administration as to one of them that the product was "generally recognized as safe" and, therefore, marketable

without an effective NDA. From that time on, FDA never challenged the marketing of these two products without effective new drug applications, and petitioner made no attempt to comply with any of the requirements in the statute or in FDA regulations which would have been applicable to "new drugs" which were "covered by effective NDA's".

Both the district court and the court of appeals in this case concluded that these two pre-1962 "me-too" products literally meet each of the three prerequisites for "grandfathered" status under Section 107(c)(4), so as not to become "new drugs" by reason of the amendment to the definition of that term. Each was marketed in the United States prior to enactment of the amendments; at that time each was generally recognized as safe and hence was not a "new drug"; and, under the literal terms of the statute, neither was "covered by an effective [new drug] application".

1. The marketing of these and petitioner's other citrus flavonoid products prior to 1962, in satisfaction of Clause (A) of Section 107(c)(4), was stipulated at trial.[25] It was further stipulated that in 1962, and at all times since, all these products have been generally recognized by qualified experts as not pharmacologically toxic in that a normal individual would not develop adverse reactions.[26] In the courts below, however, the government insisted that despite this stipulation the products were not "generally recognized as safe" within the meaning of the statute, and thus fail to qualify under Clause (B) of Section 107(c)(4), because (a) they were not generally recognized as efficacious,

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[25] A.366. The extent to which the products had been used, also stipulated (*ibid.*), was found by the district court to be "substantial" (A. 464).

[26] A. 370-71; see also Brief for Appellants Richardson *et al.*, p. 53, *USV Pharmaceutical Corp.* v. *Richardson*, No. 71-1596, 4th Cir.

and (b) in certain limited circumstances allegedly present here, a drug is unsafe for use if it is ineffective for such use.[27]

But the evidence at trial overwhelmingly demonstrated that, in any event, the necessary factual predicate for such an argument here had not been established.[28] On its own terms, moreover, the theory has never extended to "in-

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[27] It was urged that "where a drug is offered for use in the treatment of life-threatening disease", the use of "an ineffective drug * * * in the treatment of a disease where there exists a efficacious drug which is not used * * * could result in serious harm" (Brief for Appellants Richardson *et al.*, note 26 *supra*, p. 54). In its testimony before Congress on the 1962 amendments FDA had stressed that even under its view of existing law, the safety of a non-toxic drug could be construed to include efficacy *only* where the disease involved is "life-threatening" (*Hearings on S.1552 Before the Subcomm. on Antitrust and Monopoly of the Senate Comm. on the Judiciary*, 87th Cong., 1st Sess., pt. 5, at 2588 (testimony of HEW Secretary Ribicoff); *Hearings on H.R. 11581 et al. Before the House Comm. on Interstate and Foreign Commerce*, 87th Cong., 2d Sess. 64 (same)). This limitation was recognized in both of the committee reports on the 1962 amendments (S. Rep. No. 1744 (pt. 1), 87th Cong., 2d Sess. 15; H. Rep. No. 2464, 87th Cong., 2d Sess. 3). Both in 1964 and again in 1969, moreover, FDA confirmed that its theory of the pre-1962 law was applicable only under such circumstances (*Hearings on Drug Safety Before a Subcomm. of the House Comm. on Government Operations*, 88th Cong., 2d Sess., pt. 1, at 150, 183-86 (testimony of FDA Commissioner Larrick); *Hearings on Drug Efficacy Before a Subcomm. of the House Comm. on Goverment Operations*, 91st Cong., 1st Sess. 228 (testimony of FDA Commissioner Ley).

[28] The sole condition for which these products have been recommended is, as the district court found (A. 465), abnormal capillary permeability and fragility (A. 394, 396, 425), which was never suggested to be "life-threatening". It was shown that no alternative drug has been available for that condition (A. 439, 440, 442), and that petitioner's products have not been recommended to the exclusion of treatment for any underlying more serious condition (A. 428).

nocuous" drugs [29]—the very term used by the district court to summarize the testimony on the safety of these products (A. 465).[30] Indeed, FDA had advised Congress in 1962 that these very citrus flavonoid products of petitioner were among those to which the safety-includes-efficacy theory was inapplicable.[31]

Thus, the district court summarily rejected the government's contention that in 1962 these products were still in fact "new drugs" (A. 465), and the court of appeals found "no dispute that such drugs met criteria (A) and (B), as set forth in the 'grandfather clause' " (A. 468).[32] In this court the government accepts these findings, conceding that "after a full district court trial, there are now no disputed issues of fact".[33] The sole remaining controversy relates to the final prerequisite for Section 107(c)(4) "grandfather" protection, that in 1962 the products were not "covered by an effective [new drug] application".

2. As noted above, both the district court and the court of appeals concluded that each of petitioner's two "me-too"

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[29] *Hearings on S.1552,* note 27 *supra,* at 2944 (letter from HEW Secretary Ribicoff to Senate Judiciary Committee Chairman Eastland); S. Rep. No. 1744 (pt. 1), note 27 *supra,* at 16; *Hearings on Drug Efficacy,* note 27 *supra,* at 228 (testimony of FDA Commissioner Ley).

[30] In addition there was direct testimony that qualified experts would not regard the theory as applicable here (A. 426, 437, 439-40), and that, as the district court found (A. 462), the products in fact were and are generally recognized by qualified experts as safe for their intended use (A. 424-25, 437, 443). As to the efficacy of the products, the district court found that the expert witnesses called by petitioner had testified that "the plaintiff's bioflavonoids were not only safe but quite effective" (A. 465).

[31] *Hearings on S. 1552,* note 27 *supra,* at 2584 (testimony of HEW Secretary Ribicoff).

[32] Specifically as to the two "me-too" products, the court of appeals explained that they "were generally recognized as safe • • • on October 9, 1962" (A. 470).

[33] Resp. Mem., p.6 n.9.

products "meets literally the criteria for exemption" (A. 470). Unlike the district court, however, the court of appeals denied "grandfathered" status to these two products, and it did so by reading into the statute a fourth prerequisite which does not appear in its text. The court of appeals held that a drug otherwise qualifying for "grandfathered" status is ineligible for that status if it is equivalent to some other drug—a "pioneer" drug—previously marketed by the same manufacturer and which at any time prior to October 9, 1962, was the subject of an effective new drug application.

The government, confessing in this Court that the position of the court of appeals "is discriminatory and not supportable" because it would deny to petitioner's "me-too" drugs the "grandfathered" status conferred upon bioflavonoid products identical to those of petitioner but manufactured and marketed as "me-too's" by others,[34] nevertheless seeks to uphold the result as to Bivam and Duo-CVP with Vitamin K Capsules on a sweeping theory repudiated by both courts below. Under this twice-discredited theory, in determining the applicability of Section 107(c)(4) the "coverage" of an effective NDA for a single "pioneer" drug would include in its penumbra all "me-too" drugs which are "basically the same pharmacologically", regardless of the identity of the manufacturer or the method of production, even if the "me-too" was generally recognized as safe up to and including October 9, 1962 and was never itself NDA'd.[35]

Such coverage is said to flow from those "items [in the NDA] which looked to the safety of the drug as a generic article" as opposed to those giving " 'personal' information on the methods, facilities and controls which a particular company would use in its manufacture, processing and packaging."[36] (Resp. Mem., p. 10). The premise

[34] Resp. Mem., p.11 n.13.

[35] Resp. Mem., p.10.

[36] *Ibid.*

for this conclusion is that the NDA's [for pioneer drugs] "presumptively established * * * that the formulation and use covered was marketable as a general class of product",[37] so that "issuance of the pioneer's NDA normally provided the predicate for lawful marketing of the copies."[38]

B. The Theory on Which the Government Seeks Affirmance of the Judgment Below Is Refuted by the Terms and Context of the "New Drug" Provisions of the Statute and Their Contemporaneous and Consistent Construction by the Food and Drug Administration.

The government's effort to save the decision below as to Bivam and Duo-CVP with Vitamin K Capsules is fundamentally at odds with the nature of the "new drug" regulatory scheme enacted by Congress. Nothing to support it can be found in either the language or the legislative history of the 1938 Act or the 1962 amendments. Not merely does the government's present argument "represent a change" (as the Solicitor General candidly acknowledges),[39] but indeed a complete *volte-face* from FDA's own contemporaneous and long-held interpretation of the 1938 statute—of which the 1962 Congress was made well aware by the agency—as confining the "coverage" of an NDA solely to the manufacture of the precise product described, solely by the applicant, in solely the manner described in the NDA.

That the government now overreaches is "clear from the language of the Act, its legislative history, its early administrative interpretation and the construction placed upon it by Congress in subsequent enactments" (*Great Northern R. Co.* v. *United States,* 315 U.S. 262, 277 (1942)).

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[37] *Id.,* p. 11.

[38] *Id.,* p. 10. See also Petition for Certiorari, p. 14, *Richardson* v. *Bentex Pharmaceuticals, Inc.,* No. 72-555, *filed* October 5, 1972, *cert. granted,* 409 U.S. —— (1973).

[39] Resp. Mem., p. 11.

1. The government's present position is inconsistent with the intent of Congress as reflected in the precisely limited language of Section 505.

The original language of Section 505,[40] re-enacted in 1962 without change in this regard, explicitly reflects the purely "personal" nature of an effective (now, approved) NDA. Proceedings to suspend the effectiveness of an NDA were commenced by "due notice and an opportunity for hearing *to the applicant*" (Section 505(e)). Orders refusing to permit an NDA to become effective, or suspending effectiveness, were served either in person or by registered or certified mail "addressed *to the applicant or respondent*" (Section 505(g)). Judicial review was expressly authorized solely on "appeal * * * taken by *the applicant*"—originally to the district courts and since 1962 to the courts of appeals (Section 505(h)).

(a) If in 1938 Congress had intended an effective NDA to "cover" products and manufacturers not named in the application, presumably it would have recognized the adverse effect on others of an order suspending the NDA's effectiveness by giving such others—as it did in contemporaneous statutes—adequate notice, opportunity for hearing, notice of final orders, and judicial review.[41] The Food,

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[40] 52 Stat. 1052-53, *as amended*, 21 U.S.C. § 355. For the convenience of the Court, the original text of § 505 is reprinted in pertinent part at pp. 1a-3a *infra*.

[41] *Compare, e.g.*, Investment Company Act of 1940, § 40(a), 54 Stat. 842, *as amended*, 15 U.S.C. § 80a-39(a) ("Orders * * * shall be issued only after appropriate notice and opportunity for hearing. Notice to the parties * * * shall be given by personal service * * * or by registered mail * * *. Notice to interested persons, if any, other than parties may be given in the same manner or by publication in the Federal Register"); Communications Act of 1934, § 402(b), 48 Stat. 1093, *as amended*, 47 U.S.C. § 402(b):

> "Appeals may be taken from decisions and orders of the [Federal Communications] Commission * * * in any of the following cases:
>
> (1) By any applicant * * * whose application is denied * * *.

Drug, and Cosmetic Act itself contains detailed provisions for formal on-the-record rulemaking, with Federal Register publication of notices and orders, on matters where Congress intended the results of trial-type proceedings to be broadly applicable throughout an industry.[42] Yet as originally enacted, and never changed, Section 505 made no provision for notice to any other person than the applicant; for an opportunity for any other person to be heard; for notice of the final order to any other person; or for judicial review at the behest of any other person.

Nor were these provisions broadened in 1962. The same Congress which made "grandfather" protection under Section 107(c)(4) turn upon "coverage" by an effective NDA demonstrated its continued understanding of the purely "personal" coverage of an NDA by re-enacting, intact, the limited notice, hearing, service, and judicial review provision of Section 505, with their exclusive emphasis upon "the applicant" as the person adversely affected by a revocation order.[43]

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(2) By any applicant for renewal or modification • • • whose application is denied • • •.

(3) By any party to an application for authority to transfer • • • whose application is denied • • •.

• • •

(5) By the holder of any construction permit or station license which has been modified or revoked • • •.

(6) By any other person who is aggrieved or whose interests are adversely affected by any order • • • granting or denying any application described in paragraphs (1)-(4) • • •".

[42] Section 701, 52 Stat. 1055-56, *as amended*, 21 U.S.C. § 371.

[43] Federal Register publication of a § 505(e) notice of opportunity for hearing, now required by FDA regulations (21 C.F.R. § 130.14), was not provided for until after the controversy over the 1962 "grandfather" provisions had arisen (29 Fed. Reg. 7020 (1964)). Even today there is no explicit provision for Federal Register notice of final orders approving, refusing to approve, or withdrawing approval of NDA's, but merely a practice employed since about 1963.

(b) By transferring statutory review jurisdiction under Section 505(h) to the courts of appeals, while simultaneously re-enacting the provision which confers standing to seek statutory review solely upon "the applicant", the 1962 Congress further evidenced its understanding that an NDA is purely "personal" to the applicant and "covers" no one else. As the government recognizes in its argument to this Court in *Bentex*,[44] Section 505(h) confers jurisdiction on the courts of appeals only in accordance with its precise terms, which confine review to appeals by "the applicant".[45] Review of an order revoking approval of a pioneer NDA could thus be sought by a "me-too" manufacturer only in the district court, if at all, a multiplicitous pattern for judicial review which can hardly have been intended by Congress. Since it is equally inconceivable that Congress would have (or could constitutionally have) intended entirely to bar judicial review of a revocation order at the behest of a "me-too" manufacturer if his product were "covered" by another firm's NDA, the only reasonable inference is that Congress believed that only the applicant and his particular product as described in the application would be adversely affected by a revocation order, *i.e.*, was "covered" by the NDA.

(c) To say the least, moreover, serious constitutional problems of administrative due process would plainly be

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[44] Petition for Certiorari, p. 18, *Richardson* v. *Bentex Pharmaceuticals, Inc.*, No. 72-555, *filed* October 5, 1972, *cert. granted*, 409 U.S. —— (1973).

[45] See *Wholesale Grocers' Ass'n* v. *FTC*, 277 Fed. 657 (5th Cir. 1922); *Waller* v. *FTC*, No. 11,741, 4th Cir., December 6, 1967 (unreported order); *PepsiCo, Inc.* v. *FTC*, 1972 CCH Trade Cas. ¶74,260 (2d Cir. 1972) (Friendly, J.). *Cf. American Federation of Labor* v. *NLRB*, 308 U.S. 401, 404 (1940); *Cheng Fan Kwok* v. *INS*, 392 U.S. 206 (1968); *Turkel* v. *FDA*, 334 F.2d 844 (6th Cir. 1964); *Upjohn Co.* v. *Finch*, 303 F. Supp. 241, 248 (W.D. Mich. 1969). This principle was already well established at the time of the original 1938 Act. *Pote* v. *Federal Radio Commission*, 67 F.2d 509 (D.C. Cir. 1933) (*en banc*).

presented if the Act, in its original form or as amended, were construed as authorizing the Food and Drug Administration to revoke a manufacturer's authority to market his pre-1962 "me-too" product without giving him notice or hearing. This much is apparently recognized by FDA itself in the recently promulgated "regulation" which sets forth the agency's plan for implementing its new position.[46]

On the explicit premise that "an identical, similar or related drug product is covered by the NDA's for the basic product", the new regulation states in effect that NDA approval revocation orders, past as well as future, will be construed as having withdrawn marketing authority from products "identical, similar or related to" the specific products for which the NDA's were allowed to become effective. Presumably to overcome the absence of any provision in either the original or the amended Section 505(e) for extending notice and an opportunity for hearing to "me-too" manufacturers, the regulation prospectively engrafts on the statute an entirely unsanctioned procedure purporting to give such manufacturers in the future "the same opportunity as the applicant to submit data and information, to request a hearing, and to participate in any hearing".[47]

Putting aside as not presently germane the possible inadequacy even of this procedure under the Due Process Clause and the Administrative Procedure Act,[48] and the

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[46] *Applicability of DESI Notices and Notices of Opportunity for Hearing to Identical, Related, and Similar Drug Products,* § 130.40, 37 Fed. Reg. 23187 (1972).

[47] § 130.40(a), 37 Fed. Reg. 23187 (1972).

[48] According to the regulation (*ibid.*), "it is not feasible for the Food and Drug Administration to list all products which are covered by an NDA and thus subject to each notice" of opportunity for hearing on a proposal to revoke approval of an NDA which (under the regulation first promulgated in 1964, note 43 *supra*)

further constitutional difficulties in applying the new policy retrospectively to NDA revocation orders previously issued under entirely different procedures,[49] the new scheme is a classic instance of an agency's " 'attempted addition to the statute of something which is not there' " (*Commissioner* v. *Acker*, 361 U.S. 87, 93 (1959)).[50] If some such procedure would be necessary to preserve the constitutionality of the statute as construed by FDA, which the government presumably would concede, then the failure of the statute itself to provide one is persuasive evidence that Congress never intended the Act to be so interpreted. *Cf. FPC* v. *Tuscarora Indian Nation*, 362 U.S. 99, 113 (1960). And in no event should this Court reach out for an interpretation of the Act which would, by reason of the absence of any statutory provision for notice and hearing to non-applicants, put its constitutionality in doubt. *Cf. United States* v. *National Dairy Prods. Corp.*, 372 U.S. 29, 32 (1963); *Joint Anti-Fascist Refugee Comm.* v. *McGrath*, 341 U.S. 123, 165 (1951) (Frankfurter, J., concurring).

It should further be noted in this connection that marketing a "new drug" without an approved NDA in violation

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appears in the Federal Register. Yet FDA concedes that "there will be * * * areas where the judgment of experts must determine the applicability of the efficacy findings", in light of complex technical considerations as well as "any other information available on the action or properties of the drug" (37 Fed. Reg. 23185 (1972)). and suggests that any manufacturer in doubt as to whether FDA considers his product to be "covered" by another's NDA should request an advisory opinion on the matter (§ 130.40(b), 37 Fed. Reg. 23187 (1972)).

[49] Notices of opportunity for hearing in prior NDA revocation proceedings (*e.g.*, the one with respect to the products involved in this case, A. 296) recited merely the boilerplate formalism that the "applicant and any interested person who would be adversely affected by an order" could request a hearing, whereas notices issued subsequent to the new regulation explicitly refer to "manufacturers of identical, similar or related drugs".

[50] Quoting *United States* v. *Calamaro*, 354 U.S. 351, 359 (1957).

of Section 505, which under FDA's view would be the posture of a "me-too" manufacturer when approval of the pioneer NDA of another manufacturer is revoked, is a criminal offense under the Act.[51] Acceptance of the government's present position would thus effectively create by administrative regulation a new crime not prescribed by Congress. The patent Fifth Amendment problems need not be elaborated.

2. Both prior to and since the 1962 amendments, FDA has consistently construed the "coverage" of an effective NDA to be purely "personal" to the named applicant and to his product as described therein.

(a) Prior to the enactment of the 1962 Drug Amendments, there had been no suggestion either by the Food and Drug Administration or in Congress that an effective NDA "covered" anything but the specific drug described in the application as manufactured by the applicant himself. To the contrary, as early as 1941 FDA publicly advised that an NDA applied solely to a particular product of a particular manufacturer:

> "This section [505], in our judgment, applies to drugs as individual articles, not as collective groups. We have been repeatedly asked by drug manufacturers and others whether it is necessary to file an application for, let us say, sulfapyridine, when other manufacturers have already placed sulfapyridine on the market. It is our interpretation of the Congressional intent that each manufacturer of sulfapyridine or any other drug must file his own application * * *."[52]

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[51] See §§ 301(d), 303, 52 Stat. 1042, 1043, *as amended*, 21 U.S.C. §§ 331(d), 333.

[52] Statement of Theodore G. Klumpp, M.D., Chief, Drug Division, Food & Drug Admin., June 23, 1941, quoted in CCH FOOD DRUG COSM. L.REP. ¶ 71,051.09, at p. 72,039.

This restrictive view, well understood and fully accepted by industry and the bar,[53] was never relaxed. In 1960 the the Commissioner warned manufacturers that "counterfeit" drugs (manufactured as copies of existing trademarked drugs and intended to be palmed off as the original product) were for the most part "potent new drugs" and therefore required to undergo "the safety clearance procedures required for new drugs".[54] FDA's position was that a manufacturer wishing to market a drug identical to another drug, previously marketed under an effective NDA, must file his own NDA unless the product had come to be generally recognized as safe after use for a material time and extent.

"Me-too" drugs differ from "counterfeits" in that they are honestly marketed under their own names or as untrademarked "generics" (frequently at lower prices than the trademarked originals). But although their marketing might be under license from the original manufacturer if valid patents or trade secrets are involved, in other cases the original product or process was never patented, or its patent protection may have expired. And absent the consent of the original applicant, in no event has any element of the NDA—"generic" or otherwise—been thought to be the basis for marketing the "me-too". As noted in 1957, for example, FDA

> "has interpreted the statute to confer a proprietary interest in those holding effective new-drug applica-

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[53] See, *e.g.*, Kleinfeld, *New Drugs and the Durham-Humphrey Amendment*, 12 FOOD DRUG COSM. L.J. 617, 623 (October 1957) (* * * suppose one manufacturer submits a supplemental new-drug application under Section 505 for the switch [from prescription to over-the-counter availability]. This must be held in secrecy. If granted, he will, of course, have a real advantage over his competitors [marketing a similar product] until they prepare and submit their supplemental new-drug applications and the government ultimately acts on these applications").

[54] HEW Release, HEW-034, Oct. 13, 1960, quoted in CCH FOOD DRUG COSM. L. REP. ¶ 71,051, at p. 72.040.

> tions, and feels that the only way by which another can benefit from such an application is by the express consent of the person who filed it or of his duly appointed successors in interest. Failing to obtain such consent, clinical research must be conducted anew as if the conclusions shown by such research had never been proved." [55]

Thus, far from constituting or even "presumptively establishing" the right of competing manufacturers to market "me-too" products, as the government now argues (Resp. Mem., pp. 10, 11), the character of the NDA was authoritatively and consistently interpreted to have precisely the opposite effect. And this established administrative interpretation of NDA "coverage" as excluding rather than authorizing "me-too" manufacturers of "new drugs" has consistently been adhered to by the Food and Drug Administration even after the 1962 amendments. Not only does FDA require the filing of an NDA by each "me-too" manufacturer of a "new drug" "in order that we may control the labeling, the advertising that surrounds the drug, the manufacturing process that is going to be employed",[56] but reliance upon the pioneer NDA even to establish the "generic" safety and efficacy of the product is generally prohibited. As the Commissioner of Food and Drugs testified in 1967:

> "* * * under the policy FDA has followed since 1938, clinical data submitted to FDA by one firm cannot be utilized by a second firm wishing to market the same compound." [57]

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[55] Duckworth, *Some Drug Observations on the Federal Food, Drug, and Cosmetic Act*, 12 FOOD DRUG COSM. L.J. 300, 304 (May 1957).

[56] *Hearings on Present Status of Competition in the Pharmaceutical Industry Before the Subcomm. on Monopoly of the Senate Select Comm. on Small Business*, 90th Cong., 1st Sess., pt. 2, at 744 (testimony of FDA Commissioner Goddard).

[57] *Id.* at 821.

> "All the clinical trials, additional subjects studied, all the pre-clinical animal data has to be duplicated." [58]

In the words of FDA's chief counsel at that time, recently echoed by his successor, the NDA scheme presents "an individual licensing situation [rather than] a rulemaking situation".[59]

Indeed, not only reliance upon another manufacturer's NDA or some part thereof, but even mere access to it, has consistently been denied by the Food and Drug Administration. FDA has never deviated from its view that everything in the NDA file—"generic" or otherwise—is confidential and unavailable for inspection by would-be competitors or the public.[60]

It is therefore clear that from the very outset FDA has construed Section 505 of the 1938 Act as confining the "coverage" of an effective NDA to the applicant himself,

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[58] *Id.* at 744.

[59] *Id.* at 749 (HEW Ass't Gen. Counsel Goodrich); *id.*, 92d Cong., 2d Sess., pt. 22, at 8531 (HEW Ass't Gen. Counsel Hutt).

[60] *Hearings on Present Status of Competition,* note 56 *supra,* at 745-46, 748; *id.,* 92d Cong., 2d Sess., pt. 22, at 8531-32; 37 Fed. Reg. 9130 (1972) ("Since 1938, FDA has taken the position that such data ordinarily represent valuable commercial property and trade secrets that must be retained as confidential and may not be disclosed to the public"). Even under the pending proposal to expand public disclosure of FDA files (37 Fed. Reg. 9128 *et seq.* (1972)), safety and efficacy data in an approved NDA would generally remain confidential as "highly valuable material, since the law provides that a competitor cannot market or use the drug without first submitting such data and information to FDA for approval" (*id.* at 9130). The only exceptions (absent "extraordinary circumstances") would be for NDA'd products that "are 'old drugs' which do not require premarketing approval"; that are "me-too" drugs for which FDA now says an NDA, but only an abbreviated one, is necessary; and that have been removed from the market through revocation of the NDA approval. 37 Fed. Reg. at 9130.

giving no marketing authority to anyone but the applicant, and then only for the precise product described. Great weight should be given to this well-documented practice, both as the contemporaneous and long-standing interpretation of the Act by the agency charged with its administration (*e.g., Udall* v. *Tallman*, 380 U.S. 1, 16 (1965))[61] and as the agency's own contemporaneous understanding of the scope and impact of its orders allowing NDA's to become effective.[62]

(b) Nor is the controlling force of FDA's established interpretation impaired by its present assertion to the contrary for purposes of the "grandfather" issue. This Court has dealt with similar administrative turnabouts:

> "Against the [agency's] prior longstanding and consistent administrative interpretation its more recent *ad hoc* contention as to how the statute should be construed cannot stand."

United States v. *Leslie Salt Co.*, 350 U.S. 383, 396 (1956). And, in fact, FDA itself at first interpreted Section 107(c)(4) to embrace both pre-1962 "me-too's" and also their formerly NDA'd but "no longer new" pioneers,[63] and only

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[61] "Furthermore, the [agency's] interpretation gains much persuasiveness from the fact that it was the [agency] which suggested the provisions' enactment to Congress" (*United States* v. *American Trucking Ass'ns, Inc.*, 310 U.S. 534, 549 (1940). See note 147 *infra*.

[62] *Cf. Carnation Co.* v. *Pacific Westbound Conference*, 383 U.S. 213, 220-21 (1966); *Persian Gulf Outward Freight Conf.* v. *FMC*, 375 F.2d 335, 339 (D.C. Cir. 1967); *Swift & Co.* v. *FMC*, 306 F.2d 277, 281 (D.C. Cir. 1962).

[63] Interview with Deputy FDA Commissioner Harvey reported in F-D-C REPORTS ("THE PINK SHEET"), February 4, 1963, pp. 1-2. For the Court's convenience, the report of the interview is reproduced at pp. 4a-5a *infra*.

belatedly reversed its position in attempted reliance upon the theory presently advanced.[64]

The sole justification advanced by FDA for this diametric reversal of position on the "coverage" of a pre-1962 NDA is that the "statutory purpose" of the 1962 amendments "necessitated reconsideration" of the interpretation previously given to the 1938 Act.[65] But nothing in the 1962 legislation, no matter what its purpose, could retroactively change the meaning of the prior enactment (*Gemsco, Inc.* v. *Walling*, 324 U.S. 244, 265 (1945); *SEC* v. *Capital Gains Research Bureau, Inc.*, 375 U.S. 180, 199-200 (1963)).

As we show elsewhere in this brief, moreover, there is no evidence that in 1962 a different approach was intended by Congress even for the future. The Congress which enacted Section 107(c)(4) in 1962 was fully advised of the construction which had been placed upon the 1938 Act,[66] and not only failed to express the slightest dissatisfaction with that construction but evidenced continued adherence to it, both in the re-enacted portions of the "new drug" provisions[67] and in other portions of the amendments as well.[68]

Indeed, FDA's interpretation of the Act, as amended, has consistently been to the same effect as its traditional view

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[64] See PROCEEDINGS, FDA CONFERENCE ON THE KEFAUVER-HARRIS DRUG AMENDMENTS AND PROPOSED REGULATIONS, February 15, 1963, pp. 39-41, 42-43 (Gov't Printing Office 1963); Interview with Deputy FDA Commissioner Harvey, reported in F-D-C REPORTS ("THE PINK SHEET"), February 18, 1963, p. S-2. For the Court's convenience, the report of the interview is reproduced at p. 6a *infra*.

[65] Resp. Mem., p. 11.

[66] Pp. 45-46 *infra*.

[67] Pp. 27-29 *supra*.

[68] Pp. 47-51 *infra*.

when the "grandfather" clause is not under discussion.[69] And as recently as 1967 the agency rebuffed critics of its traditional position by insisting that the requirement of a complete NDA (including "generic" elements) from every "me-too" manufacturer was so firmly established that any change would have to come from Congress.[70]

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[69] (a) *Refusal to allow "me-too" manufacturers of "new drugs" to rely upon a pioneer NDA.* See *Hearings on Present Status of Competition,* note 56 *supra,* at 743-49, 754-56, 761, 821 (testimony of FDA Commissioner Goddard) (discussed at pp. 34-35 *supra*). The proposed revision of FDA's regulations on disclosure of NDA data makes clear that manufacturers wishing to market "me-too" versions of future NDA'd products will continue to be denied access to the "generic" safety and efficacy data in the pioneer NDA, until the pioneer product is no longer a "new drug" requiring a complete NDA, and that nothing in the pioneer NDA will "constitute the full reports required by statute for a competitor to obtain approval for an identical product" (37 Fed. Reg. 9131 (1972)). (b) *Records and reports.* The 1962 amendments to § 505 empowered FDA to promulgate regulations requiring regular and special reports to the agency "in the case of any drug for which an approval of an application filed pursuant to this section is in effect" (§ 505(j), 76 Stat. 782, 21 U.S.C. § 355(j)). But FDA has never suggested that "me-too" manufacturers were subject to this provision; to the contrary, the regulations apply merely to "the applicant" in the case of post-1962 drugs (21 C.F.R. § 130.13), and for pre-1962 drugs to "each applicant for whom a new drug application or supplement • • • became effective" (21 C.F.R. § 130.35)). (c) *Repackagers.* As late as 1970, FDA was unsuccessfully urging that a mere repackager of drugs purchased from the NDA applicant was required to file his own NDA in order to market "the very tablets manufactured" under the NDA held by his source (*United States* v. *Kaybel, Inc.,* 403 F.2d 1346, 1347 (3d Cir. 1970)).

[70] *Hearings on Present Status of Competition,* note 56 *supra,* at 744.

3. The government's assertion that "me-too" products were "covered" by effective NDA's filed by other manufacturers is inconsistent with the underlying principles of the Food, Drug, and Cosmetic Act.

The basic structure of the "new drug" regulatory scheme forecloses the premise on which the government has erected its present argument. Contrary to that premise, the right to market a "me-too" product without an effective NDA has never derived from an effective NDA filed by some earlier manufacturer or for some earlier product. As the court of appeals recognized (A. 472), marketability rests solely upon the fact that, through use for material time and extent, as manufactured and marketed by others, the drug involved has become generally recognized as safe (and, since 1962, as effective) and therefore is not a "new drug" within the meaning of the statute. *Cf. United States* v. *An Article of Drug * * * "Mykocert"*, 345 F. Supp. 571, 575 (N.D. Ill. 1972).

(a) The fact that an NDA has been allowed to become effective as to one manufacturer has never meant that the safety of the drug has become "generally recognized" so as to permit its marketing by another without filing an NDA of his own. As the Chief of FDA's New Drug Section wrote in 1949, whenever the statutory definition of "new drug" is applicable an NDA must be filed, even as to "drugs for which one or two new drug applications may be effective and which may be on the market":

> "The fact that an application or two applications have been permitted to become effective and that the drug is commercially available does not of necessity mean that the drug is *generally* recognized as safe for use. Rather, it means that in the opinion of the Administrator of the Federal Security Agency [of which FDA was then a component], that is to say, the medical officers of the New Drug Section, the evidence of safety for use offered by the applicant is adequate to justify a positive conclusion. But 'general recognition' is not possible until the drug has been used for a

> material time or to a material extent so that it has become generally known. In addition, in most cases the evidence on which such a positive conclusion is reached consists of observations which may be as yet unpublished by the investigators, and, therefore, not generally known to the 'experts.' "[71]

The distinction between *evidence* of safety and *general recognition* of safety is fundamental to the scheme of the "new drug" provisions of the statute.[72] It contradicts and undermines this fundamental statutory distinction, regularly insisted upon by FDA, for the government now to suggest that any element in an effective NDA "presumptively established" the marketability of the products by anyone other than the applicant, or that an effective NDA "covered" anything but the specific product as manufactured by him.

(b) It is only by ignoring the role of those elements in the NDA which are concededly "personal" to the applicant and the particular product, moreover, that the government can maintain its present position. For the "personal" elements have been central to the "new drug" regulatory scheme ever since the original enactment of the statute in 1938. If it were in fact true that "issuance of the pioneer's NDA normally provided the predicate for lawful marketing of the copies" (Resp. Mem., p. 10), then at least an NDA limited to these "personal" elements would have been required from each "me-too" manufacturer and for each "me-too" variation.

As originally enacted, Section 505 required each new drug application to include a list of the drug's compo-

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[71] Nelson, *New Drug Requirements of the Federal Food, Drug, and Cosmetic Act*, 4 FOOD DRUG COSM. L.Q. 227, 229 (June 1949) (emphasis in original).

[72] *E.g.*, *AMP, Inc.* v. *Gardner*, 389 F.2d 825 (2d Cir.), *cert. denied*, 393 U.S. 825 (1968).

nents;[73] a statement of its composition;[74] and "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug".[75] These requirements were carried forward in 1962 without change.[76]

The regulations promulgated by FDA, even prior to 1962, have always required still more details concerning the particular facilities and processes to be utilized by the applicant for the particular product involved. For example, the regulations in force at the time of the 1962 amendments required the NDA to include,

> "[i]f the applicant does not himself perform all the manufacturing, processing, packing and control operations, his statement identifying each person who will perform a part of such operations and designating the part; and a signed statement from each such person fully describing the facilities and controls he uses in his part of the operations directly or by reference." [77]

Full information was required as to serial numbers applied to raw material lots; the number of individuals checking weight or volume of ingredients as used in each manufacturing batch; "an explanation of the exact significance of any batch control numbers"; and all other details of the particular manufacturing procedures to be

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[73] Section 505(b)(2), 52 Stat. 1052.

[74] Section 505(b)(3), 52 Stat. 1052.

[75] Section 505(b)(4), 52 Stat. 1052.

[76] 76 Stat. 781, 21 U.S.C. § 355(b)(2)-(4).

[77] Section 130.4(e)(4)(b)(ii), 21 Fed. Reg. 5578 (1956). A similar provision was applicable with regard to the methods used by such third persons (§ 130.4(e)(4)(a)(iii), 21 Fed. Reg. 5578 (1956)). Equivalent provisions are currently in force (21 C.F.R. § 130.4(e)(2), ¶ 8(f)).

employed.[78] On-site inspection was required where, in FDA's judgment, a written description would not alone suffice.[79]

The particular dosage unit and form of a drug, as well as its particular combination of ingredients, have always been similarly relevant in FDA's evaluation of the drug's safety. Current administrative regulations which date from the enactment of the 1938 Act state, for example, that "the newness of a drug may arise by reason (among other reasons) of * * * (2) The newness for a drug use of a combination of two or more substances, none of which is a new drug. (3) The newness for drug use of the proportion of a substance in a combination * * *. * * * (5) The newness of a dosage, or method or duration of administration or application * * *."[80] According to FDA, timed-release dosage forms of "old drugs" may in some circumstances be "new drugs" by reason of the "possibility of unsafe overdosage if such products are improperly made and the active ingredients are released at one time or over too short a time interval".[81]

If under these criteria a particular formulation of the product is a "new drug", an NDA or supplemental NDA has been required, showing all details for that particular formulation. At the time of the 1962 amendments these included "the name and amount of each ingredient, whether active or not, contained in a stated quantity of the drug

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[78] Sections 130.4(c)(4)(b)(iv),-(vi),-(xi), 21 Fed. Reg. 5578 (1956.) The current requirements on these matters are in 21 C.F.R. § 130.4(c)(2), ¶¶ 8(e),-(j),-(o).

[79] Sections 130.6, 25 Fed. Reg. 12595 (1960). The current equivalent is at 21 C.F.R. § 130.6.

[80] C.F.R. § 130.1(h), first promulgated in 3 Fed. Reg. 1847 (1938).

[81] 21 C.F.R. § 3.512, first promulgated at 24 Fed. Reg. 3756 (1959).

in the form in which it is to be distributed"; "the methods used in processing and packing each proposed dosage form"; "a representative sample or samples of the finished dosage form(s) proposed in the application and employed in the clinical investigations"; and "a representative sample or samples of finished market packages of each dosage form of the drug prepared for initial marketing, and if any such sample is not from a commercial scale production batch, in addition such a sample from a representative commercial scale production batch".[82]

Even after the NDA becomes effective, variations in these respects have been required not merely to be reported but to be approved in advance. The regulations in force now and at the time of the 1962 amendments require each applicant under an effective NDA to submit a supplemental NDA "for any change beyond the variations provided for in the [original] application (including changes in the scale of production such as from pilot-plant to production batch) that may alter * * * the identity, strength, quality, or purity of the drug * * *."[83] Only if the product was no longer "new", and the applicant's "me-too" variation was not itself a "new drug", was the applicant free to market the variation without an effective supplemental NDA therefor.[84]

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[82] Sections 130.4(c)(3),-(4)(a)(ii), 21 Fed. Reg. 5578 (1956); §§ 130.4(c)(5)(a)(i),-(ii), 26 Fed. Reg. 2595 (1961). Today a separate NDA must be filed for each dosage form of a "new drug" (21 C.F.R. § 130.4(d)(ix)).

[83] 21 C.F.R. § 130.9(a)(2), first promulgated in 21 Fed. Reg. 5579 (1956).

[84] Section 130.9(e), 25 Fed. Reg. 12595 (1960). This provision was first promulgated in 21 Fed. Reg. 5579 (1956), and was deleted, without notice (compare the notice of proposed rulemaking at 29 Fed. Reg. 2790 (1964)), only after the controversy with respect to the 1962 "grandfather" provisions had arisen (29 Fed. Reg. 7020 (1964)).

The reason for requiring such information, and its review by FDA, both in the original NDA and on a continuing basis, is obvious. Every ingredient of a drug product may affect its safety.[85] The quantities of particular ingredients in a dosage unit, the relative proportions of each ingredient, and the method of administration are equally relevant to safety.[86] And to evaluate the safety of a drug as produced by a particular manufacturer it is necessary to evaluate, in the words of the regulations, "the adequacy of the manufacturing, processing, and packing methods to determine and preserve the identity, strength, quality, and purity of the drug".[87] As FDA itself noted in its comments to the Senate Judiciary Committee on the bill which became the Drug Amendments of 1962, "the methods, facilities and controls used by a particular drug manufacturer bear importantly on the safety of the drug".[88]

(c) Despite the importance to the public of the regulatory measures governing these "personal" aspects of manufacturing products covered by effective NDA's, at no time prior to 1962 did the Food and Drug Administration ever suggest that the manufacturer of a "me-too" product was required to file an NDA with respect thereto, or to wait for such an NDA to become effective before commencing

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[85] The fatal properties of "Elixir Sulfanilimide", which were responsible for the original enactment of the "new drug" provisions in 1938 (see note 147 *infra*), were contributed by the "supposedly inert" solvent or carrier for the therapeutic ingredient. Nelson, note 71 *supra*, 4 FOOD DRUG COSM. L.Q. at 227.

[86] *Id.* at 230.

[87] Section 130.4(a), 21 Fed. Reg. 5577 (1956).

[88] Letter from HEW Secretary Ribicoff to Senator Eastland, dated September 13, 1961, in *Hearings on S. 1552*, note 27 *supra*, at 2943. See also *Hearings on Present Status of Competition*, note 56 *supra*, at 755-56 (1967 testimony of FDA Commissioner Goddard to the same effect).

marketing. To the contrary, the regulations in 1962 did not require supplemental NDA's for "me-too" variations marketed even by the pioneer applicant, if the product was no longer "new" (*i.e.*, was generally recognized as safe) and the variation was not itself a "new drug".[89]

"Me-too" products nevertheless could not lawfully have been marketed without such controls had they been required, which would have been the case if the authority for their marketing was an effective NDA. The Food and Drug Administration practice of not imposing such controls thus confirms the basic principle, hitherto accepted by all, that "me-too's" were marketed as "old drugs" on the authority of general recognition of their safety, and demonstrates that the predicate for the present argument that they were covered by the NDA's approved as to pioneer manufacturers is wholly unsupportable.

4. Congress was expressly advised by FDA in the course of considering the 1962 amendments that an effective NDA was purely "personal" to the applicant and, while significantly amending the "new drug" provisions, left them unchanged in this respect when it incorporated the concept of "coverage" by an effective NDA into the "grandfather" provisions of Section 107(c)(4).

Congress would in any event be presumed, absent contrary evidence, to have intended the "grandfather" provisions of Section 107(c)(4) to be construed with reference to the law as it then stood. *St. Louis I.M. & S.R. Co.* v. *United States*, 251 U.S. 198, 207 (1920). But if there were any doubt in this instance as to the legislative intent, it would be resolved by the clear and direct notice which Congress was given by the Food and Drug Administration itself that NDA's were purely "personal".

(a) The formal report of the Department of Health, Education and Welfare on S. 1552, the bill which became

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[89] Section 130.9(e), 25 Fed. Reg. 12595 (1960).

the Drug Amendments of 1962, was a letter from HEW Secretary Ribicoff to Senate Judiciary Committee Chairman Eastland. The letter unequivocally stated, in describing the "new drug" regulatory scheme then in force, that:

> "If two or more manufacturers propose to market the same 'new drug' each must file a clearance application, the underlying reason being that the methods, facilities, and controls used by a particular drug manufacturer bear importantly on the safety of the drug".[90]

The same premise was implicitly reflected in other FDA testimony on S. 1552. As originally introduced by Senator Kefauver, S. 1552 would have initiated the licensing of each and every drug manufacturer on a product-by-product basis.[91] The Food and Drug Administration opposed this provision, on the grounds that the "personal" elements of an effective NDA already included the equivalent of such a licensing system for "new drugs" and that all other drugs could adequately be controlled if the agency were given authority to promulgate regulations defining "good manufacturing practices" enforceable in post-marketing seizure, injunction and criminal proceedings.[92]

The clear premise of this testimony was that all drugs being manufactured outside the scope of the "personal" elements in an effective NDA were "old drugs", as to which the proposal for judicially enforceable "good manufacturing practice" regulations was necessary in order to insure the integrity of manufacturing facilities, processes, and controls. It would have been entirely inconsistent with this premise for Congress to have thought that any products then on the market were "covered by effective

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[90] *Hearings on S. 1552*, note 27 *supra*, at 2943.

[91] Section 4(a)(13), S.1552, 87 Cong., 1st Sess.

[92] *Hearings on S. 1552*, note 27 *supra*, at 2591 (testimony of HEW Secretary Ribicoff).

NDA's" except those specifically being regulated through the "personal" elements of an effective NDA.[93]

(b) The construction contemporaneously put upon a statute by its administrators "carries most weight when the administrators participated in drafting and directly made known their views to Congress in committee hearings" (*Zuber* v. *Allen*, 396 U.S. 168, 192 (1969); see also *Perkins* v. *Matthews*, 400 U.S. 379, 391-94 (1971)). Having thus been told in 1962 that NDA's were purely "personal", each manufacturer of a "new drug" being required to file his own NDA, Congress (1) re-enacted the heavily-amended "new drug" provisions without change in this regard, and (2) employed the concept of "coverage by an effective NDA" in the "grandfather" provisions of Section 107(c)(4). The Food and Drug Administration can hardly now suggest that Congress nevertheless had something else silently in mind. *Farmers Educational & Coop. Union* v. *WDAY, Inc.*, 360 U.S. 525, 533 (1959).

5. The terms of the 1962 amendments demonstrate Congress' recognition of the purely "personal" character of the NDA, and explicitly distinguish the "generic" certification regulations by which the safety and efficacy of antibiotic drugs are controlled.

Finally, Congress' reliance upon the Food and Drug Administration's long-held view as to the purely "personal" coverage of an effective NDA was reflected in the 1962 amendments not merely in the re-enactment of Section 505 without change in this respect, but also in the amendments relating to the antibiotic regulatory provisions and to the control of animal feed.

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[93] See, *e.g.*, 108 Cong. Rec. 21057 (remarks of Representative Schenk, who was the author of the amended "good manufacturing practices" provision) ("Before any manufacturer is permitted to make a new drug he must file complete details of his manufacturing process with the Food and Drug Administration").

(a) *Antibiotics.* As amended in 1962, Section 507 of the Act directs FDA to promulgate regulations of general applicability establishing such standards of identity, potency, quality and purity as necessary to insure the safety and efficacy of antibiotic drugs, and requires FDA certification of all such drugs on a batch-by-batch basis.[94] Antibiotic drugs "subject to Section 507" are exempt from the NDA requirements of Section 505.[95] Provision is made for regulations exempting any antibiotic "drug or class of drugs" from the batch certification requirement when "not necessary to insure safety and efficacy of use".[96]

As originally enacted Section 507 applied solely to penicillin products, to which four specifically named additional antibiotics were subsequently added by legislation.[97] In 1962 the provision was expanded to include all present and future antibiotics.[98] The use of generally applicable regulations promulgated pursuant to the on-the-record rulemaking provisions of the Act to establish the "generic" elements of safety and efficacy was continued, however. The result is that, unlike manufacturers of other drugs requiring pre-marketing scrutiny, who have "private licenses", the manufacturers of antibiotic drugs "have

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[94] Section 507(a), 59 Stat. 463, *as amended*, 21 U.S.C. § 357(a). See *United States* v. *An Article of Drug* • • • *Bacto-Unidisk*, 394 U.S. 784, 785-87 (1969).

[95] Section 507(e), 59 Stat. 463, *as amended*, 21 U.S.C. § 357(e).

[96] Section 507(c), 59 Stat. 463, *as amended*, 21 U.S.C. § 357(c). Exemption is also authorized for antibiotic drugs manufactured for storage, processing, labeling or repacking by another, for use in manufacturing other drugs, and for investigational use (§ 507 (d), 59 Stat. 463, *as amended*, 21 U.S.C. § 357(d)).

[97] 61 Stat. 21 (streptomycin); 63 Stat. 409 (aureomycin (renamed chlortetracycline by 67 Stat. 389), chloramphenicol, and bacitracin).

[98] Drug Amendments of 1962, §§ 105(a)-(b), 76 Stat. 785, 21 U.S.C. §§ 357(a), -(b).

public regulations in the form of a monograph so once the drug is approved anyone can make the drug." [99]

Thus, a manufacturer proposing to market an antibiotic already on the market need file merely the equivalent of the "personal" data in an NDA.[100] For it is the regulations which establish for all manufacturers the marketability of particular classes of antibiotic drugs.

Prior to 1962, the statute was not explicit as to the regulatory status of antibiotic drugs exempted from batch certification, beyond the reverse implications of the provision exempting from the requirements of Section 505 "any drug subject to Section 507". The 1962 amendments clarified this ambiguity by explicitly excluding from the Section 505 exemption any "new drug exempted from the requirements of this section [507] * * * pursuant to regulations".[101] To permit compliance with the NDA requirements of Section 505 for an antibiotic "drug or class of drugs" thus exempted by regulation from Section 507, a proviso was added to Section 507(e) that:

> "for purposes of section 505, the initial request for certification, as thereafter duly amended, pursuant to section 507, of a new drug so exempted shall be considered a part of the application filed pursuant to section 505(b) *with respect to the person filing such request and to such drug* as of the date of the exemption." [102]

Like the "grandfather" provisions of Section 107(c)(4), this proviso first appeared in the version of S.1552 reported

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[99] *Hearings on Present Status of Competition*, note 56 *supra*, 92d Cong., 2d Sess., pt. 22, at 8531 (testimony of HEW Ass't Gen. Counsel Hutt).

[100] The procedural regulations prescribing the data required to be filed by a new manufacturer are at 21 C.F.R. § 146.2(b).

[101] § 105(e), 76 Stat. 786, 21 U.S.C. § 357(e).

[102] *Ibid.* (emphasis added).

by the Senate Judiciary Committee. It clearly reflects, we submit, the Committee's and Congress' understanding that, unlike an antibiotic regulation, an effective NDA was purely "personal" to the named applicant and was not authority for anyone else to market even an identical product.

(b) *Animal feed.* In 1958 Congress had comprehensively amended the Food, Drug, and Cosmetic Act to control the manufacture and use of substances used in the production and processing of food, including animal feed.[103] The new regulatory provisions were made inapplicable, however, to substances "used in accordance with a sanction or approval granted" pursuant to the Act prior to the effective date of the amendment.[104] Prior sanctions and approvals included, of course, NDA's which had been allowed to become effective.[105]

In accordance with its general policy that an effective NDA was purely "personal" to the applicant, from the beginning the Food and Drug Administration interpreted this "grandfather" provision in the Food Additives Amendment to protect only the applicant himself when the prior sanction or approval relied upon was an effective NDA.[106] By 1962 it was the practice of FDA to confine even the applicant's "grandfathered" status to his use of the precise manufacturing facilities and processes described

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[103] Food Additives Amendment of 1958, 72 Stat. 1784, 21 U.S.C. §§ 321 *et seq.*

[104] Section 2, 72 Stat. 1784, 21 U.S.C. § 321(s)(4).

[105] See H. Rep. No. 1761, 86th Cong., 2d Sess. 87 (HEW explanation of proposed amendments to Food Additives Amendment of 1958).

[106] *Hearings on H.R. 7624 et al. Before the House Comm. on Interstate and Foreign Commerce*, 86th Cong., 2d Sess. 73 (testimony of HEW Secretary Flemming); *id.* at 85 (testimony of FDA Commissioner Larrick).

in the NDA.[107] Yet because FDA was barred by the "Delaney Clause" in the Food Additives Amendment from approving any additive for general use which in experiments could be found to induce cancer,[108] some useful animal feed additives could be produced only by firms with a pre-1958 effective NDA therefor.[109]

To remedy this discrimination, in 1962 the animal feed industry proposed to modify the "Delaney Clause" by allowing useful but carcinogenic substances to be approved as animal feed additives if no residue would remain in edible portions of the animal.[110] The Food and Drug Administration had long supported such a revision.[111] After receiving the endorsement of the House Commerce Committee,[112] the proposal was included in the Drug Amendments of 1962 [113] for the precise purpose of eliminating the discrimination complained of,[114] further confirming the understanding of the 1962 Congress that an effective NDA was purely "personal" to the applicant.

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[107] See, *e.g.*, 108 Cong. Rec. 21080 (Representative Rogers of Florida).

[108] Section 4, 72 Stat. 785, *as amended*, 21 U.S.C. § 348(c)(3)(A). A similar clause had also been included in the Color Additive Amendments of 1960, § 103(b), *as amended*, 21 U.S.C. § 376(b)(5)(B).

[109] See *Hearings on H.R. 7624*, note 106 *supra*.

[110] *Hearings on H.R. 11581*, note 27 *supra*, at 401 (statement of Animal Health Institute).

[111] See *Hearings on H.R. 7624*, note 106 *supra*.

[112] H. Rep. No. 2464, 87th Cong., 2d Sess. 11.

[113] Sections 104(f), -(g), 76 Stat. 785, 21 U.S.C. §§ 348(c)(3)(A), 376(b)(5)(A).

[114] 108 Cong. Rec. 21077-82 (House); *id.* at 22039 (Senate).

C. To Give Effect to Section 107(c)(4) in Accordance With Its Terms, and Thus To Confirm the "Grandfathered" Status of Petitioner's "Me-Too" Products Under the Amended Definition of "New Drug", Would Be Consistent With the Expressed Purposes of This Aspect of the 1962 Amendments and With the Character of the Act's Bifurcated Regulatory Scheme.

1. The 1962 amendment to the statutory definition of "new drug" was not intended to affect drugs already on the market and not being regulated by the Food and Drug Administration as "new drugs", but simply to insure that any new claims for such products would be treated identically with claims for future products not yet on the market.

Virtually the exclusive preoccupation of the sponsors of the 1962 amendments was with the need to subject *future* drugs (and future claims for existing drugs) to pre-marketing scrutiny by FDA for efficacy as well as safety.[115] The legislative history is bereft of any comprehensive statement by the sponsors, or by the Congressional committees which considered the legislation, setting out with precision the extent to which FDA review would be required as to existing claims for drugs already being sold.

Three points, however, emerge with clarity. *First*, the inclusion of "grandfather" provisions in addition to those enacted in 1938 establishes that reliance would continue to be placed solely upon misbranding actions to eliminate false or misleading efficacy claims for at least some post-1938 products already on the market. *Second*, both the Food and Drug Administration and the Congress explicitly noted their unwillingness to require FDA pre-marketing control of existing "old" drugs in the even more critical context

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[115] This is apparent from the emphasis placed throughout on the fact that, under the proposed legislation, FDA scrutiny of efficacy claims would occur *prior* to marketing (*e.g.*, H. Rep. No. 2464, note 27 *supra*, at 3), a concept which could have no relevance to claims already being made for products already on the market.

of safety. *Third,* the single and limited purpose of amending the statutory definition of "new drug"—the amendment whose applicability is in issue here—was simply to assure that future claims for existing products and claims for future products added after their initial marketing, as well as all claims for entirely new products, would be subjected to pre-marketing scrutiny by FDA. There is no evidence whatsoever of any legislative intention to impose "new drug" controls for the first time on existing claims for existing products such as "me-too's" which, as to those claims, were "old drugs" generally recognized as safe.

(a) As first reported by the Senate Judiciary Committee, the bill which ultimately became the Drug Amendments of 1962 [116] made no change whatever in the definition of "new drug", although as originally proposed by Senator Kefauver the bill would have changed the definition to include drugs not generally recognized as effective. The Committee's omission was deliberate.

Some members disagreed directly with the suggestion that new claims for previously approved products should require advance clearance by FDA. As Senator Hruska put it:

> "The change would also cause confusion when a new use is discovered for a safe old drug. For example, if aspirin in its normal dosage were to be newly recommended as efficacious for acne, it should not have to go through the elaborate new-drug procedure. If FDA believes the claim is false, it has ample power to seize the drug as 'misbranded' under existing law." [117]

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[116] S. 1552, 87th Cong., 1st Sess.

[117] 108 Cong. Rec. 10108. Senator Hruska further stated that a change would be "unnecessary to give FDA power to pass on the efficacy of truly new drugs, which are covered by the existing definition because, being new, they are not generally recognized to be safe" (*ibid.*).

Senator Kefauver argued strongly against the movement to delete his proposed amendment of the "new drug" definition. But the sole ground for his objection was that new claims for previously approved products *should* require separate pre-marketing approval by FDA, which ought not to be required to bring its challenges to new claims by way of enforcement actions under the misbranding provisions of the Act.[118]

The formal report of the Senate Judiciary Committee on S. 1552 replied directly to Senator Kefauver's stated objection. Explaining why the proposal to amend the "new drug" definition was unnecessary, the Committee observed that any new claim for a previously approved product *would* in fact require FDA pre-marketing approval, even without a change in the "new drug" definition:

> "any such new use would have to be submitted under a supplemental new drug application and would have to be cleared for safety under existing law, and for safety and effectiveness under the law as it would be amended." [119]

The dissenters from the Committee decision not to amend the "new drug" definition merely reiterated Senator Kefauver's original objection. In their view, it was necessary to expand the definition if the provisions for substantial evidence of efficacy were "to have any real force", but only because

> "otherwise the requirement would only apply to the initial claims made for a drug and not to later claims made after the initial new drug application had been approved." [120]

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[118] 108 Cong. Rec. 10278.

[119] S. Rep. No. 1744 (pt. 1), note 27 *supra*, at 17.

[120] *Id.* at 34 (views of Senators Kefauver *et al.*).

(b) While S. 1552 was pending in the Judiciary Committee, Europe's tragic thalidomide episode received widespread publicity. Attention to this incident increased after S. 1552 was reported, and the White House promptly proposed further amendments to the bill.[121] The Judiciary Committee responded with a supplemental report endorsing the White House proposals. These included expansion of the "new drug" definition to include drugs not generally recognized as effective, as urged by Senator Kefauver. But the sole basis assigned for the change was "to eliminate any possible ambiguity"

> "on the question • • • as to the circumstances and extent to which a new claim or change of claim for effectiveness made after the initial approval of a new-drug application could be made without supporting evidence to be submitted to [FDA] under the new-drug procedure." [122]

On the floor of the Senate, Senator Eastland as Chairman of the Judiciary Committee described the effect of the definitional change in similarly limited terms. The Senator explained that, as a result of the change, "every brand new product, and every *new claim* for an existing product, would be subject to the tests and procedures established" for FDA review of new drug applications.[123] He referred to no other result expected to flow from the change in defi-

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[121] See 108 Cong. Rec. 15692 *et seq.*

[122] S. Rep. No. 1744 (pt. 2), 87th Cong., 2d Sess. 5 (emphasis added). It was with regard to this point that the report noted in the very next sentence that the amended bill would "require • • • all claims for effectiveness, whether made initially in a new-drug application or at any time thereafter", to be approved by FDA prior to marketing.

[123] 108 Cong. Rec. 17366 (emphasis added). See also 108 Cong. Rec. 22050 (statement of Senator Kefauver on supplemental Judiciary Committee report, inserted at his request "to further aid in the understanding of the legislative history", *id.* at 22044).

nition of "new drug". There was no suggestion that FDA approval would have to be obtained as to any existing claims for products already on the market, including "me-too" products, which were then "old drugs" generally recognized as safe. After similarly narrow explanations in the House,[124] the revised S. 1552 was enacted.

(c) As first proposed by Senator Kefauver in April 1961, S. 1552 had contained neither "effective date" nor "grandfather" provisions of any kind. In the House, the principal vehicle for consideration of the Food, Drug, and Cosmetic Act amendments proposed in S. 1552 was the White House-backed H.R. 11581.[125] As introduced in May 1962 by Representative Harris, the Administration bill would have retained the 1938 definition of "new drug" only for "any drug with respect to which an [NDA] was effective" at the time the amendment was enacted, and even then only until such time as approval of the NDA was revoked on any ground, including the new ground of inefficacy or substantial doubt as to efficacy.[126]

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[124] The post-thalidomide report of the House Commerce Committee on the principal House bill (H.R. 11581), which also proposed to amend the definition, echoed the Senate report in stating merely that "this change requires that all claims for effectiveness, whether made initially in a new drug application or at any time thereafter, must be supported by 'substantial evidence' "(H. Rep. No. 2464, note 27 *supra*, at 8). The definitional change was not discussed further; no additional reason for the change was expressed by the committee or its members; and no further anticipated result of the change was ever identified.

[125] 87th Cong., 2d Sess. Hearings (note 129 *infra*) had been held on the House companion to S. 1552 (H.R. 6245, 87th Cong., 1st Sess.) by the House Committee on the Judiciary, to which it had been referred, but the bill was never reported.

[126] Section 108(c). See *Hearings on H.R. 11581*, note 27 *supra*, at 26 (report of Dep't of HEW).

As already noted (p. 54 *supra*), in its July 1962 report on S. 1552 the Senate Judiciary Committee proposed deletion of the amendment to the "new drug" definition.[127] The subsequent White House proposals included not merely reinstatement of such an amendment, but also the limited and temporary "grandfather" provisions of the Harris bill in the House.[128]

Industry witnesses thereafter testifying on H.R. 11581 continued to oppose amendment of the "new drug" definition, on the grounds already endorsed by the Senate Judiciary Committee.[129] It was urged as to the efficacy amendments generally that in any event:

> "There should be a specific provision that the new requirement of 'effectiveness' shall not apply to old drugs already on the market or to new drugs which were cleared before the amendment, and such new drugs should be subject to withdrawal or suspension [of the NDA] only on safety grounds." [130]

One industry witness proposed a "grandfather" clause for the amendment to the "new drug" definition which would parallel the "grandfather" provision in Section 201(p)(1) of the 1938 Act (p. 60 *infra*).[131] The Food and Drug Administration, on the other hand, opposed "a complete

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[127] S. Rep. No. 1744 (pt. 1), note 27 *supra*, at 17.

[128] Amendment No. 4(g)(2), 108 Cong. Rec. 15696.

[129] *E.g., Hearings on H.R. 11581*, note 27 *supra*, at 237-38 (testimony for Pharmaceutical Mfrs. Ass'n), 367-68 (testimony for Proprietary Ass'n). See also *Hearings on H.R. 6245 Before the Antitrust Subcomm. of the House Comm. on the Judiciary*, 87th Cong., 2d Sess., ser. 32, at 450 (statement of Pharmaceutical Mfrs. Ass'n), which preceded the first report of the Senate Judiciary Committee.

[130] *Hearings on H.R. 11581*, note 27 *supra*, at 236 (testimony for Pharmaceutical Mfrs. Ass'n).

[131] *Id.* at 368-69 (testimony for Proprietary Ass'n).

grandfather clause", suggesting merely "a reasonable transition provision." [132]

(d) The second report of the Senate Judiciary Committee, which reinstated the amendment to the "new drug" definition (p. 55 *supra*),[133] adopted neither the across-the-board "grandfather" provisions urged by industry nor the White House/FDA proposal to apply the new definition to existing "old drugs" without significant restriction. The Committee substitute, which was subsequently endorsed by the House [134] and ultimately enacted into law as the "grandfather" provision for the amended definition of "new drug",[135] confers "grandfathered" status on products which at enactment of the amendment met three conditions:

(A) that the drug "was commercially used or sold in the United States";

(B) that the drug was not a "new drug" under the definition then in force, *i.e.*, the original 1938 definition; and

(C) that the drug "was not covered by an effective [new drug] application".[136]

Under this apparent compromise the new definition was made applicable, in furtherance of its purpose, (a) to new

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[132] *Id.* at 573. While this statement was not formally transmitted to the House Commerce Committee until August 30, 1962, it is reasonable to assume that the same position was earlier communicated to the Senate Judiciary Committee during FDA's appearances (see, *e.g.*, 108 Cong. Rec. 14679) at the executive sessions of that Committee to consider the White House proposals for further amendment of S. 1552 as reported (see S. Rep. No. 1744 (pt. 2), note 122 *supra*, at 1).

[133] S. Rep. No. 1744 (pt. 2), note 122 *supra*, at 5.

[134] See H. Rep. No. 2464, note 27 *supra*, at 12.

[135] H. Rep. No. 2526, 87th Cong., 2d Sess. 23 (conference report).

[136] Section 107(c)(4), 76 Stat. 789, 21 U.S.C. note foll. § 321.

claims for existing products and (b) to all claims for future products, whether made in the original NDA or subsequently added. The White House/FDA proposal was partially implemented, but without going beyond the limited reach of that purpose, which had never extended to the imposition of "new drug" controls on existing claims for products such as "me-too's" already being marketed as "old drugs". Thus, the applicability of the amended definition was expanded further, but only to those existing products which were already being regulated or were already required to be regulated under the "new drug" provisions of the 1938 Act, *i.e.*, to products which were still "new drugs" or which, even if no longer "new", were still "covered by an effective [new drug] application".

The Senate Judiciary Committee report accordingly noted that "in the case of a drug on the market which was never subject to the new-drug procedure before, the amendments to the new-drug definition relating to drug effectiveness would not apply to existing labeling claims".[137] The brief comments in the House Commerce Committee report on H.R. 11581 [138] and in the House-Senate conference report [139] precisely echo the Senate report.

(e) Thus, the legislative evolution of neither the "grandfather" provisions of Section 107(c)(4) nor the amended "new drug" definition whose applicability it controls can furnish support for applying the amended definition to pre-1962 "me-too" products for which NDA's had never been filed. We have already shown (pp. 53-56 *supra*) that the Congressional purpose in amending the definition was a clear, narrow and limited one—to insure that "an NDA'd drug would not make new, unsupported claims of

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[137] S. Rep. No. 1744 (pt. 2), note 122 *supra*, at 8.

[138] H. Rep. No. 2464, note 27 *supra*, at 8.

[139] H. Rep. No. 2526, note 135 *supra*, at 23.

efficacy".[140] As this Court long ago stated (*Pacific Mail S.S. Co.* v. *Joliffe*, 2 Wall. 450, 459 (1864)):

> "in construing * * * Acts of amendment * * * it is necessary to observe great caution to avoid giving an effect to these Acts which was never contemplated by the Legislature".

Section 107(c)(4) should not be construed so narrowly that the amendment of the "new drug" definition is given an effect never intended or even contemplated by Congress, and contradicted by its express terms.

2. The government's proposed construction of Section 107(c)(4) would add nothing to what is already provided by the 1938 "grandfather" provision in Section 201(p) itself.

The contrary course now advocated by FDA, particularly when taken together with positions being advanced by the agency on related issues, would render Section 107(c)(4) mere surplusage, adding nothing to the original "grandfather" clause contained since 1938 in the "new drug" definition itself.

The 1938 clause exempts entirely from the "new drug" definition any product which was on the market prior to 1938 so long as it continues to be recommended for the same uses.[141] It is evident from Congress' addition of Section 107(c)(4), therefore, that protection was also in-

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[140] Note, *Drug Efficacy and the 1962 Drug Amendments*, 60 GEO. L.J. 185, 197 n.73 (1971).

[141] "[A] drug not [generally] recognized [as safe and effective for its intended uses] shall not be deemed to be a 'new drug' if at any time prior to enactment of this Act it was subject to the Food and Drug Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; * * *."

Section 201(p)(1), 52 Stat. 1041, *as amended*, 21 U.S.C. § 321(p)(1).

tended to be given to at least some products which had come on the market between 1938 and 1962. The government's reading of Clause (C) of Section 107(c)(4) would nevertheless exclude (1) all products for which a pre-1962 NDA became effective, and (2) all products identical, similar, or related to such an NDA'd product.

This leaves only non-NDA'd post-1938 products which were totally unknown for the pharmaceutical use claimed upon first being introduced. Yet ever since 1938 the term "new drug" has included (a) products without the requisite "general" recognition, and (b) products enjoying such recognition but which have not been used for a material time and to a material extent. *Cf. United States* v. *An Article of Drug* * * * *"Bentex Ulcerine"*, 469 F.2d 875, 880 (5th Cir. 1972).[142]

It would be a contradiction in terms to suggest that a post-1938 drug, which when introduced was unlike any other product already on the market, could then have been

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[142] FDA is presently contending, moreover, that general recognition by qualified experts within the meaning of the statute is impossible in the absence of a body of clinical studies and published literature (compare, *e.g., United States* v. *Forty-One Cases*, 420 F.2d 1126, 1130 (5th Cir. 1970) with *United States* v. *An Article of Drug* * * * *Excedrin P.M.*, CCH FOOD DRUG COSM. L. REP. ¶ 40,486 (E.D.N.Y. 1971). Indeed, the government is presently asking this Court to rule that "there can be no general recognition of safety and effectiveness in the absence of 'substantial evidence' of effectiveness" as defined in the statutory criteria for NDA approval, *i.e.*, "adequate and well controlled investigations, including clinical investigations" (§ 505(d), 76 Stat. 781, 21 U.S.C. § 355(d)). See Memorandum for Respondents, p. 7, *Hynson, Westcott & Dunning, Inc.* v. *Richardson*, No. 72-414, *filed* November 3, 1972, *cert. granted*, 409 U.S. — (1973). While these contentions have been made with reference to "general recognition" under the "new drug" definition of the Act as amended in 1962, at least with regard to drug effectiveness, the standard of "general recognition" dates from 1938 and was not amended or even considered in 1962.

"generally" recognized as safe or "used to a material extent or for a material time" before being marketed.[143] No such product could lawfully have been marketed without an effective NDA, which according to the government would disqualify it for "grandfathered" status. If the government is correct in its over-all view of the 1962 amendments, therefore, Section 107(c)(4) is a nullity serving no function whatever.[144]

To suppose that Congress intended this result would ignore "the basic axiom—that courts should construe all legislative enactments to give them some meaning" (*Rosado* v. *Wyman*, 397 U.S. 397, 415 (1970)). And it is no answer to say that the "purpose" of the 1962 amendments in general so requires. Quite aside from the much more limited purpose of the change in definition of "new drug",[145] and Congress' demonstrated rejection of FDA's proposal to deny "grandfathered" status to all products brought on the market between 1938 and 1962,[146] it is the precise function of *any* "grandfather" clause to limit the applicability of statutory changes made in pursuance of

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[143] Nor is it reasonable to think that any previously unknown product put on the market after 1938 without an effective NDA, and thus in violation of law, would thereafter have been studied in "adequate and well controlled investigations, including clinical investigations", so as to satisfy by 1962 the statutory test as for "old drug" status as construed by FDA (note 142 *supra*). The shortage of qualified clinical investigators has frequently been recognized even by FDA itself. *E.g., Hearings on Present Status of Competition*, note 56 *supra*, at 764, 821 (testimony of FDA Commissioner Goddard).

[144] Nor is it to be supposed that Congress intended to confer "grandfathered" status under Section 107(c)(4) solely upon pre-1962 products which had first come on the market unlawfully, in violation of the criminal prohibition against marketing a "new drug" without an effective NDA (see note 51 *supra*).

[145] See pp. 53-56 *supra*.

[146] See pp. 56-59 *supra*.

some general purpose. As this Court held with reference to the statute of limitations in the Longshoremen and Harbor Workers' Compensation Act (*Pillsbury* v. *United Engineering Co.*, 342 U.S. 197, 200 (1952)):

> "We are aware that this is a humanitarian Act, and that it should be construed liberally to effectuate its purposes; but that does not give us the power to rewrite the statute of limitations at will, and make what was intended to be a limitation no limitation at all".

3. The government's interpretation of Section 107(c)(4) ignores the bifurcated nature of the regulatory scheme created by Congress, and in practical effect would cancel Congress' deliberate choice in 1962 not to require administrative approval by FDA for the continued marketing of all post-1938 drug products, in reliance upon post-marketing civil and criminal misbranding actions as to those post-1938 products which in 1962 were being regulated only as "old drugs".

(a) Contrary to what the government would imply (Resp. Mem., p. 9), Congress did *not* intend in 1962 to require the efficacy of all marketed drugs to be established in administrative proceedings before the Food and Drug Administration. Ever since the original enactment of the statute in 1938 Congress has differentiated between "new drugs" and "old drugs", choosing to regulate the marketing of the latter solely through civil and criminal post-marketing actions for the enforcement of a variety of statutory prohibitions.

Under the 1938 Act the category of "new drug" included only products brought on the market subsequent to enactment of the statute which were "not generally recognized * * * as safe" for their intended uses.[147] The term did not

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[147] Section 201(p), 52 Stat. 1041. The "new drug" provisions of the Act were proposed by, and apparently drafted in, the Food and Drug Administration in the wake of a drug tragedy while the bill was nearing final passage. See *United States* v. *An Article of Drug * * * Bacto-Unidisk*, 394 U.S. 784, 798 (1969) and legislative material there cited.

encompass pre-1938 products no matter what their safety status. The public was protected against unsafe "old drugs" through seizure, injunctive and criminal actions for misbranding, which was defined to prohibit as "misbranded" all drugs dangerous to health when used as directed in the labeling.[148]

This differentiation for regulatory purposes between "new drugs" and "old drugs" was carried forward intact in the 1962 amendments. Administrative control of "new drugs" was expanded to include the requirement that efficacy as well as safety must be proved prior to marketing, and to authorize administrative revocation of marketing authority when efficacy can no longer be established.[149] But the "grandfather" clause in Section 201(p)(1) protecting pre-1938 products was left intact, so that all such products would continue entirely outside the regime of administrative pre-marketing controls without regard to general recognition of either their safety or their effectiveness. And, through Section 107(c)(4), more recently introduced drugs—brought onto the market since 1938 as "old drugs" without having gone through the "new drug" procedure [150] and which in 1962 were still generally recognized as safe—were allowed to remain on the market sub-

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[148] Section 502(j), 52 Stat. 1051, 21 U.S.C. § 352(j). *E.g.*, *United States* v. *Lanpar Co.*, 293 F. Supp. 147 (N.D. Tex. 1968).

[149] Drug Amendments of 1962, §§ 102(b)-(d), 76 Stat. 781-82, 21 U.S.C. §§ 355(b), -(d), -(e).

[150] S. Rep. No. 1744 (pt. 2), note 122 *supra*, at 8; H. Rep. No. 2464, note 27 *supra*, at 8; H. Rep. No. 2526, note 135 *supra*, at 23 (conference report); 108 Cong. Rec. 17366 (Senator Eastland, Chairman of the Judiciary Committee which considered and favorably reported the bill).

ject solely to civil and criminal actions for misbranding to eliminate false or misleading claims of efficacy.[151]

The Senate Judiciary Committee characterized as "ample" the "power" available to FDA through these proven remedies in the case of existing claims for products already on the market and generally recognized as safe, concluding that as to such products nothing more was required.[152] As already shown (pp. 53-56 *supra*), the Committee's subsequent recommendation to amend the definition of "new drug" was intended simply to make clear that *new* claims for "old drugs" or for previously approved "new drugs" would require advance FDA approval, in no way departing from its earlier and continuing position that the misbranding remedies were sufficient as to *existing* claims for "old drugs".

Congress thus evidenced its decision to impose only post-marketing regulation such as this on existing "old drugs" such as "me-too's". Indeed, this choice was further reflected, with the endorsement of the Food and Drug Administration itself, in the even more critical context of safety.

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[151] Section 502(a), 52 Stat. 1050, 21 U.S.C. § 352(a). *E.g.*, *United States* v. *Detroit Vital Foods, Inc.*, 407 F.2d 570 (6th Cir. 1969), *rev'd in part on other grounds sub nom. United States* v. *Kordel*, 397 U.S. 1 (1970). We are advised that nothing in the petition for certiorari in *Hynson, Westcott & Dunning, Inc.* v. *Weinberger* (No. 72-414) was intended to deny that a misbranding action under § 505(a) would lie against such products, despite the government's apparent reading of the petition to the contrary (Memorandum for the Respondents in No. 72-414, pp. 4-5 n.2), and no such suggestion would be well taken. Section 107(c)(4) grants exemption only from the 1962 change in definition of "new drugs", and false or misleading efficacy claims have constituted unlawful "misbranding" since 1938.

[152] S. Rep. No. 1744 (pt. 1), note 27 *supra*, at 17.

S. 1552,[153] the bill which became the Drug Amendments of 1962, would have regulated drug manufacturing and quality control procedures by creating a licensing system for producers of prescription drugs, in which particular establishments would be licensed to produce particular drugs.[154] The testimony of Secretary Ribicoff on S. 1552 denied the necessity for any such system. The Secretary pointed out that the objectives of such a licensing system could be achieved, as to "old" drugs, through an "alternative approach" in which "adulterated" drugs would be defined to include drugs "prepared in inadequate manufacturing facilities, with inadequate personnel, or without adequate control procedures * * * [as] determined by conditions imposed in advance by general regulations."[155]

The mechanism for enforcing compliance with good manufacturing practices as prescribed by regulation, Secretary Ribicoff noted, would be seizure of products produced in violation of the regulations; injunctions against their distribution; and criminal prosecution of the manufacturer involved. The manufacture of "new drugs", on the other hand, would continue to be controlled by requiring the NDA to contain "advance proof" of adequate manufacturing facilities and control procedures.[156]

The licensing system proposed by Senator Kefauver was accordingly rejected, in reliance upon the Secretary's disclaimers.[157] In this way, for purposes of regulating quality control, Congress again deliberately chose to differentiate between "new drugs" and "old drugs", and in the case of "old drugs" to rely upon civil and criminal enforcement

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[153] 87th Cong., 1st Sess.

[154] S. 1552, 87th Cong., 1st Sess., § 4(a)(13).

[155] *Hearings on S. 1552*, note 27 *supra*, at 2591.

[156] *Ibid.*

[157] S. Rep. No. 1744 (pt. 1), note 27 *supra*, at 12; Drug Amendments of 1962, § 101, 76 Stat. 780, 21 U.S.C. § 351(a)(2).

actions rather than pre-marketing approval by FDA in this important area of drug safety.

It would therefore simply obliterate the deliberate distinction drawn by Congress between "new drugs" and "old drugs", and its choice of a separate regulatory mechanism for the latter, to expand the "new drug" provisions of the Act to cover this case. As the Third Circuit noted in rebuffing a similar attempt of the Food and Drug Administration to do so, "other procedures exist within the broad reach of other provisions of the Act which safeguard against" the consequences feared by the agency, in that "misbranding [is] specifically prohibited" (*United States* v. *Kaybel, Inc.*, 430 F.2d 1346, 1347 (1970)).

(b) At bottom, we submit, it is simple dissatisfaction with the clearly expressed intent of Congress which underlies the government's assertion that "me-too" products were "covered" by the effective NDA's governing other manufacturers or other versions of the product. But "neither [this Court] nor the Commissioner may rewrite the statute simply because we may feel that the scheme it creates could be improved upon" (*United States* v. *Calamaro*, 354 U.S. 351, 357 (1957)).

The Food and Drug Administration apparently now believes it would be better, from a regulatory standpoint, if "me-too" products as well as NDA'd products marketed prior to 1962 were subject to the amended definition of "new drug". And so it might seem to some legislators if confronted with the issue.

> "Legislation introducing a new system is at best empirical, and not infrequently administration reveals gaps or inadequacies of one sort or another that may call for amendatory legislation. But it is no warrant for extending a statute that experience may disclose that it should have been made more comprehensive."

Addison v. *Holly Hill Fruit Prods., Inc.*, 322 U.S. 607, 617 (1944).

But the statute which Congress did enact in 1962 preserves the pre-1962 definition of "new drug" for all products which in 1962 were already on the market, were not "new drugs" under that pre-amendment definition, and were not "covered by an effective NDA". There can be no doubt that as understood by Congress this included "me-too" products, by whomever manufactured, including the two manufactured by petitioner.

As the Second Circuit observed with respect to yet another FDA request for a judicial *tour de force* to remedy alleged statutory defects:

> "The case fits perfectly Mr. Justice Brandeis' famous stricture, 'What the Government asks is not a construction of the statute, but, in effect, an enlargement of it by the court, so that what was omitted, presumably by inadvertence, may be included within its scope.'"

Toilet Goods Ass'n. v. *Finch*, 419 F.2d 21, 29 (2d Cir. 1969)).[158] To apply the amended definition of "new drug" to these two products of petitioner would be "to do what the legislative branch of the Government failed to do or elected not to do"—an act of legislation which "is not within * * * [this Court's] province" (*Hanover Bank* v. *Commissioner*, 369 U.S. 672, 688 (1962)).

II. THE COURT OF APPEALS ERRED IN HOLDING THAT, DESPITE THE "GRANDFATHER" PROVISIONS OF THE 1962 AMENDMENTS, THE AMENDED DEFINITION OF "NEW DRUG" APPLIES TO PETITIONER'S FORMERLY NDA'D PRODUCTS WHICH BY 1962 WERE NO LONGER "NEW DRUGS" AND WERE NO LONGER BEING REGULATED AS "NEW DRUGS".

The second category of drugs involved in this case consists of five citrus flavonoid products first marketed by petitioner in 1956 and 1957 under effective NDA's. The district court ruled that these products also enjoy "grand-

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[158] Quoting *Iselin* v. *United States*, 270 U.S. 245, 251 (1926).

fathered" status under Section 107(c)(4). Finding that in 1962 the products were on the market and were no longer "new drugs", thus qualifying under Clauses (A) and (B) of the "grandfather" provisions,[159] the court went on to find that petitioner's actions subsequent to the time the NDA's became effective—endorsed or acquiesced-in by FDA—amounted in practical terms to withdrawal of the NDA's prior to the effective date of the amendments.[160] Thus, the district court concluded, in 1962 the formerly NDA'd products were no longer "covered by an effective application" and the Clause (C) criterion for "grandfathered" status was met.

The court of appeals disagreed. In its view, there had been no provision in the statute for an applicant's "withdrawal" of his NDA once it became effective; the only "withdrawal" contemplated is withdrawal of *approval* by FDA, under the authority of Section 505(e), and here approval had not been withdrawn (A. 469). Thus, the court

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[159] The court of appeals held that "so much the defendants seem to concede" (A. 469), and in this Court the government does not dispute the point (see pp. 23-24 *supra*). There is no question that an NDA'd product can through time become no longer "new", as FDA's own regulations in 1962 recognized (§ 130.9, 25 Fed. Reg. 12595 (1960); see p. 43 *supra*). See *Hearings on Present Status of Competition*, note 56 *supra*, 92d Cong., 2d Sess., pt. 22, at 8530 (HEW Ass't Gen. Counsel Hutt).

[160] See pp. 6-7 *supra*. The district court found (A. 464-65):

> "The plaintiff made that clear through its correspondence with the Federal [sic] Drug Administration. It then ceased compliance with the submittal of data and new labeling, as required by the Federal Drug Administration for products covered by effective NDA's—The record further discloses that the Federal Drug Administration advised the plaintiff in writing that its products covered by [two of the NDA's] were not new drugs—and it was stipulated that the compound in these two products is identical to the bioflavonoid compound in plaintiff's other products and that the recommended uses of all the [bioflavonoid] products are essentially the same".

of appeals concluded, each of these originally-NDA'd products remained "covered by an effective application" on the date of the 1962 amendments.

A. The Statute Has Never Precluded Withdrawal of a New Drug Application by the Applicant as Found To Have Occurred in This Case.

1. The root error of the court of appeals was in confusing withdrawal of the *application,* as found by the district court, with withdrawal of *approval,* as presently authorized by Section 505(e). The court may have been misled by its apparent belief [161] that the acronym "NDA" stands for "New Drug Approval" rather than "New Drug Application". But the belief was mistaken, and in logic the authority of FDA since 1962 to withdraw *approval* of the application has nothing to do with the right of the applicant to withdraw the underlying application itself.

As the government recognizes, moreover, "prior to the 1962 amendments, FDA itself had no authority to withdraw" (Resp. Mem., p. 8). The statute spoke in terms of FDA authority to issue orders "suspending the effectiveness of the application".[162] The *expressio unius* approach relied upon by the court of appeals [163] and by the government [164] to deny petitioner's pre-1962 capacity to withdraw its applications is thus entirely inapplicable here.

2. Nor did the substance of FDA's pre-1962 powers foreclose the capacity of the applicant to withdraw his appli-

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[161] *Bentex Pharmaceuticals, Inc.* v. *Richardson,* 463 F.2d 363, 365 n.2 (4th Cir. 1972), *cert. granted,* 409 U.S. — (1973) (No. 72-555) (A. 259). *Cf. Hynson, Westcott & Dunning, Inc.* v. *Richardson,* 461 F.2d 215, 217 (4th Cir. 1972), *cert. granted,* 409 U.S. — (1973) (Nos. 72-394, 72-414) (A. 173).

[162] Sections 505(e), -(h), 52 Stat. 1053.

[163] A. 469.

[164] Resp. Mem., p. 8.

cation as no longer needed at some time after it had become effective. As the court of appeals recognized in upholding the jurisdiction of the district court to entertain this action, FDA has always been wholly without authority to consider or decide in Section 505(e) proceedings whether a previously-NDA'd product continues to be a "new drug", and that issue could never have been raised by either party to a Section 505(e) proceeding.[165] Section 505(e) could never have been invoked by petitioner, moreover, and not even by FDA to terminate NDA "coverage" on the ground that the product had become "generally recognized as safe" and therefore no longer required the regulatory controls imposed on NDA'd products. Section 505(e) has always been a provision of limited scope, permitting the Food and Drug Administration to move against an NDA only for the very opposite substantive reason—that the evidence no longer shows the product to be safe (or, under the amended statute, effective) and hence no longer allows the product to be marketed.

3. To use the recent words of counsel for the Food and Drug Administration, pre-1962 NDA's are "obsolete or inactive" when "the drug has become an old drug".[166] Common sense says that an effective NDA which thus became superfluous may and should have been retired on that ground. Because the statute prescribed no particular procedure for doing so, one must be inferred from the whole scheme and purpose of the Act "if it is to be treated as a working instrument of government and not merely as

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[165] The government currently attacks that ruling in *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, No. 72-555, and defends the contrary view of the Third Circuit in *CIBA Corp.* v. *Weinberger*, No. 72-528. The government's position is also supported by the petitioner in *Hynson, Westcott & Dunning, Inc.* v. *Weinberger*, No. 72-414.

[166] *Hearings on Present Status of Competition*, note 56 *supra*, 92d Cong., 2d Sess., pt. 22, at 8530 (HEW Ass't Gen. Counsel Hutt).

a collection of English words" *United States* v. *Dotterweich*, 320 U.S. 277, 280 (1943)). And it strains both common sense and reason for the government now to deny that a pre-1962 NDA became "obsolete or inactive" when the "old drug" status of a product was asserted by the manufacturer, ratified by FDA, acted upon by the manufacturer (in discontinuing supplemental NDA's), and acquiesced-in by the agency (in no longer imposing NDA controls).

B. Regardless of Whether Petitioner Could Lawfully Have "Withdrawn" Its Applications After They Became Effective, Under the Facts as Found by the District Court, Its Formerly NDA'd Products Were No Longer Covered by an Effective NDA in 1962.

In any event, the court of appeals' preoccupation with whether petitioner had the "right" to "withdraw" its NDA's misconceived the critical inquiry. Regardless of how the district court had formulated the issue, the question on appeal was not whether petitioner had withdrawn its NDA's, or indeed even whether petitioner had a "right" to "withdraw". Properly stated, the true question was whether petitioner's bioflavonoid products which had earlier been NDA'd were, on October 9, 1962, still "covered by an effective [new drug] application".

Even prior to 1962, the function of the NDA was not exhausted when the application became effective. An effective NDA was considered by the Food and Drug Administration to be "an official legal document" which "defines in no uncertain terms the indications, contraindications, cautions, dosage and basic professional literature", "to break the terms of [which] is to court trouble".[167] Accordingly, manufacturers of drugs covered by effective NDA's

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[167] Holland, *Current Drug Problems Under the Federal Food, Drug, and Cosmetic Act*, 11 FOOD DRUG COSM. L.J. 486, 489 (September 1956). The cited author was then Medical Director of FDA.

were obligated by the regulations then in force [168] to report all changes in the composition, manufacturing facilities or processes, quality controls, and labeling of such products and to obtain advance approval from the Food and Drug Administration if the change would be significant.

The purpose of this reporting and approval requirement was to enable FDA to continue its regulatory function after an NDA became effective. As the Deputy Commissioner of Food and Drugs stated in 1955:

> "Evaluation of [safety] evidence does not end with the initial marketing of the drug. Up to this point, it has been produced in small quantities and restricted to the use of investigators qualified to perform the scientific testing necessary to establish its safety. Experience in widespread use may require label changes, and mass production may result in improvement of manufacturing facilities." [169]

The district court relied upon the sequence of events between the time petitioner's NDA's became effective and the date of the 1962 amendments for its finding of practical and effective withdrawal of the NDA's prior to October 9, 1962, and on this basis concluded that thereafter petitioner's formerly NDA'd products were no longer "covered". In its preoccupation with the abstract question whether petitioner lawfully could "withdraw" its NDA, the court below ignored the underlying facts on which the district court relied, which showed that by 1962 the products involved were no longer being treated by either the manufacturer or FDA as subject to the continuing regulatory controls applicable to NDA'd products. These facts, we submit, surely justified the district court's ultimate conclusion that on October 9, 1962, the products were no longer "covered" by an effective NDA.

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[168] Section 130.9, 25 Fed. Reg. 12595 (1960).

[169] Harvey, *Administration of the Food, Drug, and Cosmetic Act*, 10 Food Drug Cosm. L.J. 441, 446 (July 1955).

However characterized, the nub of what happened here was that through the actions of both petitioner and FDA, taken together, the NDA's were inactivated and by 1962, despite their former status, the products involved had become no longer "covered by an effective [new drug] application" within the meaning of Clause (C) of Section 107(c)(4). Had Congress intended to apply the amended definition of "new drug" to products such as these, it would have conferred "grandfathered" status only where the drug "was not a new drug" under the 1938 Act and "*had never been* covered by an effective application". But Congress in fact legislated differently, and as the district court held, the "grandfather" provisions which it did enact embrace petitioner's formerly NDA'd but no longer "new" and no longer "covered" products.[170]

C. To Apply Section 107(c)(4) to Petitioner's Formerly NDA'd Products Would Be Consistent With the Purpose of the 1962 Amendment to the "New Drug" Definition and Would Not Make Surplusage of Any Portion of the Statute.

We have already shown that Congress' purpose in amending the definition of "new drug" was solely to insure FDA pre-marketing scrutiny of (1) future claims for existing products and (2) claims first made for future products subsequent to approval of the original NDA (pp. 53-56 *supra*). There is no evidence, as we have seen, that Congress intended to impose "new drug" controls on existing claims for products already on the market which were not then being regulated as "new drugs".

There can accordingly be no warrant in the purposes of the amendments for failing to recognize the "grandfathered" status conferred upon petitioner's formerly NDA'd but no longer "new" products under Section

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[170] Because the court of appeals relied upon these NDA's to deny "grandfathered" status to petitioner's "me-too" products, reinstatement of the district court's holding on this point would *a fortiori* require reversal as to the "me-too" products as well.

107(c)(4). Indeed, the Food and Drug Administration itself so interpreted Section 107(c)(4) immediately after its enactment, and only subsequently decided upon its present contrary position.[171] As FDA thus originally recognized, the remedy for allegedly false or misleading efficacy claims for such formerly NDA'd products is a misbranding action, as contemplated by Congress, in the same manner as all other "old drugs" under Congress' bifurcated regulatory scheme.

It is true that, as the court of appeals stressed (A. 470), the only specific reference in the legislative history of Section 107(c)(4) is to products "that have never been subject to the new-drug procedure". But there is nothing to suggest that this and similar comments were intended comprehensively to catalogue or exhaust the circumstances in which Section 107(c)(4) would be applicable, or that the authors had in mind that precise group of pre-1962 products, such as petitioner's, which had once been subject to "new drug" procedures but which had then become no longer "new" and which, additionally, had ceased to be regulated as "new drugs" by FDA.[172]

Nor does this conclusion make "surplusage" of Clause (C), as the court below feared (A. 469). It is not our position that the fact that an NDA'd product had become

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[171] Notes 63-64 *supra*.

[172] The two-year freeze imposed by Section 107(c)(3), which temporarily barred proceedings under the amended § 505(e) to revoke approval of effective pre-1962 NDA's so as to allow the applicants thereunder to compile their evidence, serves an entirely different function from Section 107(c)(4). The two-year provision was intended to apply to "a new drug already on the market" (S. Rep. No. 1744 (pt. 2), note 122 *supra*, at 8; 108 Cong. Rec. 22039 (Senator Kefauver explaining House-Senate conference report); *cf.* H. Rep. No. 2464, note 27 *supra*, at 12), whereas Section 107(c)(4) deals with products which in 1962 were not "new drugs".

generally recognized as safe and no longer "new", standing alone, automatically inactivated the NDA. We assume *arguendo* that there must be some further action which removes the product from new-drug regulation, before it can be found the product is no longer "covered" by an effective NDA.

Here, however, FDA had not only ruled that the products were generally recognized as safe, and thus "not new", but the agency had unambiguously acquiesced in petitioner's withdrawal of these products from "new drug" regulatory procedures. FDA's own actions in connection with those of petitioner established that the products were no longer "covered." According to the district court, it was necessary for petitioner to show these additional facts in order to satisfy the criterion for exemption prescribed by Clause (C). Under no view of the statute as interpreted and applied by the district court, therefore, can Clause (C) be considered surplusage.

CONCLUSION

The judgment of the court of appeals should be reversed as to each of petitioner's citrus flavonoid products, both formerly NDA'd and "me-too", for the reasons stated in Point II above (pp. 68-76). As to petitioner's "me-too" products, Bivam and Duo-CVP with Vitamin K Capsules, the judgment should be reversed for the addditional and wholly separate reasons stated in Point I (pp. 21-68).[173]

Respectfully submitted,

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[173] On the ground that "there are now no longer any disputed issues of fact in the present case", the government has abandoned its thus-far-unsuccessful challenge to the district court's exercise of jurisdiction to hear and decide this case on the merits (Resp. Mem., p. 6 n.9). However, if this Court were to hold in *CIBA Corp.* v. *Weinberger* (No. 72-528) that the government is correct in its view that, in cases such as this, "the primary jurisdiction doctrine may oblige courts to defer to FDA" (*ibid.*), then the appropriate disposition of this case might be to vacate the judgment of the court of appeals, and to remand to the district court with directions to dismiss without reaching the merits, so as to allow petitioner to contest *de novo* the alleged "new drug" status of its citrus flavonoid products in the still-pending NDA approval revocation proceeding. For if the Court were generally to require primary adjudication of "new drug" status before FDA, it would seem illogical, if not impermissible under the statutory scheme as thus construed, to apply a different rule in the present case merely because the issue has already been adjudicated in the district court without benefit of an FDA determination on the record.